Self-Referential Processing in the Adolescent Brain: Do Neural Self-Referential Processes Related to Adolescent Self-Concept Confer Risk for Depression?

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Adolescence is an important developmental period in which self-concept stabilizes and depression develops. During early adolescence, self-concept becomes reliant on social comparison, leading to excessive self-focused attention that may contribute to risk for depression. Research has confirmed that negative global and social self-concept are closely related to the development of depressive symptoms during adolescence. Affective neuroscience studies demonstrate that there is a neural network underlying the processing of self-related information, yet little is known about how its function is associated with subjective feelings of self-concept and risk for depression in adolescence. The current study examined whether neural functioning during negative, compared to positive, self-referential processing is associated with early-adolescent girls' ratings of global and social self-concept and depressive symptoms at two timepoints. The final sample included 39 girls (M_{yrs}=12.18, SD=.77) who reported on their social and global self-concept using a questionnaire and during a functional neuroimaging task in which they responded whether they believed positive and negative personality trait words were true about them. Girls reported on depressive symptoms at the time of the scan and 6-months later. Results showed that greater social self-competence was related to greater neural activation when processing self-negative, relative to self-positive, adjectives in the PCC/precuneus, superior temporal gyrus/temporoparietal junction, and inferior parietal lobe. More positive self-perceptions during the imaging task were related to greater activation to self-positive>self-negative in the visual association area. More depressive symptoms at T1 were associated with greater activation to self-negative>self-positive in the caudate/putamen, dorsal anterior cingulate/supplementary motor area, and somatosensory cortex/inferior parietal cortex, while more symptoms at T2 were related to greater insula activation. Indirect effects analyses revealed that more negative self-perceptions during the fMRI task explained the positive association between dorsal medial prefrontal cortex activity in response to negative traits and depressive symptoms. This may suggest that youth with hyperactivation in the dMPFC during self-referential processing of negative traits may be excessively focused on negative self-related information. Findings highlight how differential neural processing of negative versus positive self-relevant information directly maps onto behavioral reports of self-concept during adolescence and how these brain-behavior associations may contribute to depression in early-adolescence.

Table of Contents

List of Tables

List of Figures

1.0 Introduction

Epidemiological and longitudinal studies have unanimously shown that risk for major depressive disorder (MDD) increases substantially between childhood and adolescence, with up to 50% of teens reporting significant depressive symptoms and prevalence rates for MDD rising to approximately 14-20% (see reviews by Birmaher et al., 1996; Costello, Copeland, & Angold, 2011; Hankin, 2006). Individual self-concept plays an important role in adolescents' psychosocial adjustment and maladjustment, including depression. Self-concept is a complex psychosocial construct that encompasses self-perceptions about personal qualities, evaluative information about one's competence within various domains, as well as attitudes towards the self (Marsh & Shavelson, 1985). Although self-concept begins developing in childhood, adolescence is a crucial period in which youth's attitudes regarding competencies and worth begin to stabilize (Cole et al., 2001; Shapka & Keating, 2005).

Fluctuations in self-perceptions during adolescence are normative (Cole et al., 2001); however, persistently low self-concept, including low domain-specific self-competencies and self-worth, is detrimental to psychological trajectories and is a known causal and maintaining factor of depression (Harter & Jackson, 1993; King, Naylor, Segal, Evans, & Shain, 1993; Lewinsohn, Rohde, & Seeley, 1998; Sowislo & Orth, 2013). Early-to-mid adolescents are especially vulnerable to declines in self-perceptions due to the major transitions that occur during this period and due to adolescents' high reliance on others' perceptions for self-validation (Cole et al., 2001; Rankin, Lane, Gibbons, & Gerrard, 2004; Sontag, Graber, & Clemans, 2011; Wigfield, Eccles, Iver, Reuman, & Midgley, 1991). Therefore, early-to-mid adolescence may be a crucial period to investigate the neural mechanisms related to underlying self-perceptions or self-concept that influence the increased risk of depressive symptoms and clinical depression disorders. The term "depression" will be used hereon to denote both symptoms and clinical disorders.

Self-concept plays an important role in adolescent development, as it is found to be associated with a range of positive psychosocial outcomes in youth, including: greater motivation to achieve (Covington, 1984; Ryan & Deci, 2000); positive psychological adjustment (Marsh, Parada, & Ayotte, 2004); and better peer relations (Deković & Meeus, 1997; Salmivalli & Isaacs, 2005). Specifically, self-concept is a construct posited to be hierarchical in nature (Harter, 1982). Accordingly, self-concept encompasses lower-order level domain-specific self-competencies, in which regard for the self is distinct and variable for a variety of life domains (Harter, 1982). Adolescents use knowledge and evaluative information regarding their abilities (e.g., academic, social, physical, and athletic) to create feelings of self-competency within these domains (Harter, 1982). Domain-specific self-perceptions are then posited to guide adolescents' attitudes towards the self on a higher-order or global level (i.e., self-worth or self-esteem) (Harter, 1982; Marsh & Shavelson, 1985; Rosenberg, 1965). It is theorized that self-concept begins to develop in early childhood, and is dependent on significant others' approval and rejection responses to help shape the child's personality traits, attributes, and behavior (Harter, 1999). This may make early adolescence an important time to investigate the mechanisms underlying the development of self-concept, given that by early adolescence, youth are defining themselves through social comparison and interpersonal characteristics (Harter, 1990). Also, cognitive ability becomes more fluid and abstract with age, facilitating a shift in the development of self-concept. During this shift, self-concept becomes more dynamic and differentiated across domains; however, globally, it also becomes more stable as youth learn to assess commonalities of traits across interaction experiences (Harter, 1990, 1999). Therefore, it is believed that early adolescence is a time in which working models or cognitive representations of youth's roles, competencies, and sense of worth become internalized which begin guiding their self-beliefs within interactions in future contexts (Harter, 1999).

Unfortunately, because early adolescence is the time in which self-concept starts to become instantiated as part of an individual's identity, substantial and prolonged decreases in self-concept during the early-adolescent period put youth at this age at a particularly high risk for the development of depression. According to the established cognitive theory of depression, persistently low self-worth and negative beliefs about the self are causal and maintaining factors in depression (Beck, 1967). Beck's proposed theory has been upheld by a large body of research, including a recent meta-analysis that included 77 longitudinal studies (19 utilizing adolescent samples) (Sowislo & Orth, 2013). Results showed that low self-esteem was a significant predictor of depression onset and severity, rather than solely a correlate or a residual symptom of depression (Sowislo & Orth, 2013). In addition to the effects of low global self-worth/esteem, several studies have also shown that adolescents' perceptions of competence within interpersonal or social domains are also highly associated with depression (Evans, 1994; King et al., 1993; Marsh et al., 2004; Seroczynski, Cole, & Maxwell, 1997; Tram & Cole, 2000; Vannucci & Ohannessian, 2017). Based on the increasingly salient effects of social relationships on psychological well-being during early adolescence, including self-concept (Steinberg & Morris, 2001), this evidence suggests that the combination of low self-competence in the social domain and low global self-worth may be particularly detrimental to adolescents' risk for depression.

Cognitive models of depression have emphasized that individuals who experience depression likely have a cognitive predisposition or vulnerability (Kovacs & Beck, 1978). Although, evidence specific to negative self-worth cognitions may help to support this theory

(Sowislo & Orth, 2013), it also may be that depressed affect leads to negative cognitions (Coyne & Gotlib, 1983). Coyne and Gotlib (1983) posited that differences in cognitive attributions and biases found between depressed and non-depressed individuals may be due, not specifically to trait-like cognitive biases per se, but rather to the differences in cognitive biases as a function of diverse prior salient experiences. With regard to cognitive biases specific to the self, the manner in which researchers should operationalize cognitive biases posited by Coyne and Gotlib is similar to symbolic interactionist theory on the development of self-concept, which states that important social interactions shape the development of adolescents' cognitive biases in self-perceptions (Harter, 1999; Shrauger & Schoeneman, 1979). Consequently, it may be that because of previous social interactions, by early adolescence some youth could have developed either: 1) more negative and less positive biases in self-related cognitions/schemas; or 2) an exaggerated salience or awareness of inner self-related thoughts and feelings, more generally. In either case, these self-related schemas may make these youth particularly vulnerable to the development of depression following times of significant stress or challenges in which negative self-related biases become especially salient and highly activated (Ingram & Smith, 1984; Teasdale, 1983; Teasdale & Dent, 1987). Research investigating the neural underpinnings of such cognitive predispositions in the processing of self-related information during early adolescence and how they associate with risk for future depression may help to elucidate a neurodevelopmental model of self-concept and risk for the onset of depression during the mid-adolescent period. The current paper proposes to test this aim in a sample of early adolescents not yet diagnosed with depression.

Although rates of depression begin to rise in early adolescence, particularly for girls, they do not peak until later in adolescence—around the ages 15-16 years old (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). Therefore, it may be that research investigating *risk and/or* *vulnerability* for depression should focus on the early-adolescent years. More specifically, early adolescence is time in which significant declines in self-perceptions generally occur, in part due to the occurrence of major transition (e.g., pubertal maturation, volatile and changing social environment, academic advancement) and youth's high concern about and reliance on others' perceptions when formulating their own self-perceptions (Cole et al., 2001; Rankin et al., 2004; Wigfield & Eccles, 1994). Given that low self-concept is a key risk factor for depression, early adolescence may be an especially important period in which to investigate the possible neurobiological risk factors underlying self-perceptions. Investigating these neurobiological factors could help explain how the mechanisms underlying the development of self-concept are associated with the onset of adolescent depression.

1.1 Role of Self-Referential Neural Functioning in Self-Concept and Depression

Research from the affective neuroscience literature in adults has suggested that the medial prefrontal cortex (MPFC; including dorsal and ventral regions), the anterior cingulate cortex (ACC; BA24/25), the posterior cingulate cortex/precuneus (PCC/precuneus; BA7/31), and the inferior parietal lobe (IPL; BA39/40) extending into the temporoparietal junction (TPJ; BA22) may be core regions particularly important to processing self-relevant information (Frewen et al., 2020; Northoff et al., 2006). For example, several of these regions, commonly referred to as cortical midline structure including the MPFC, the PCC/precuneus, and the posterior region of the parietal cortex (PPC), have been and shown to activate as a unit consistently across self-referential processing tasks, regardless of stimuli domain (i.e., verbal, memory, social, or emotional stimuli) (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Davey, Pujol, & Harrison, 2016;

Molnar-Szakacs & Uddin, 2013; Northoff et al., 2006). While it has been suggested that the MPFC plays the most important role in distinguishing self from other (Araujo, Kaplan, & Damasio, 2013), through graph-analytic and intrinsic functional connectivity techniques, activation in both the anterior MPFC and the PCC/precuneus has been found to be core to all self-related cognition (Andrews-Hanna et al., 2010). Additionally, research has shown that these regions are most activated when individuals are asked to reflect on aspects of their psychological selves (e.g. personality traits, autobiographical memories, and self-knowledge) (Molnar-Szakacs & Uddin, 2013). Further differentiation has also become evident between the functionality of these two core regions (Davey et al., 2016). Specifically, the functionality of the MPFC is believed to involve regulating sensory and semantic self-representations, directing ongoing thought processes, and guiding decisions about whether to attend to internal or external stimuli, while the PCC is posited to focus mental representations of the self through the use of autobiographical memory when attending to self-relevant information (Davey et al., 2016; Whitfield-Gabrieli & Ford, 2012).

In addition to the two core regions of self-referential processing, other regions implicated in social-cognitive processing, including the inferior parietal lobe (IPL) and temporoparietal junction (TPJ), have also been found to be important to self-referential processing across adolescence and adulthood (Davey et al., 2016; Molnar-Szakacs & Uddin, 2013). From the adult literature, the IPL is speculated to retrieve and integrate complex semantic information that helps to contribute to ones sense of self, while the TPJ is implicated in the integration of attention, memory, language, and perception to construct social context to guide decision making and behavior (Carter & Huettel, 2013). Furthermore, the TPJ is speculated to be part of a subsystem, along with the dorsal MPFC (dMPFC) and other lateral temporal regions, that is associated with self-judgments about current mental states and situations and the utilization of introspection of preferences, feelings, and emotions for self-relevant processing (Andrews-Hanna et al., 2010). The IPL may be part of a separate subsystem, which includes the ventral MPFC (vMPFC), hippocampal regions, and the retrosplenial cortex (oriented just ventral to the PCC and posterior to the parahippocampus), and is implicated more during self-judgements about near-future oriented situations and use of episodic memory, imagination, and scene construction during self-referential processing (Andrews-Hanna et al., 2010).

Although these regions may play different functional roles, research has suggested a model in which they are functionally connected during self-referential processing. Specifically, using dynamic causal modeling techniques, researchers have found that during self-referential processing the PCC exerts a positive influence both directly and indirectly, through the IPL, on the MPFC, and in turn the MPFC exerts a negative influence on the PCC (Davey et al., 2016). A separate study using transcranial direct current stimulation suggested similar connectivity patterns between these regions (Kajimura, Kochiyama, Nakai, Abe, & Nomura, 2016). The results of these studies may suggest that when attending to self-relevant information, activation begins within the PCC to help an individual focus on cognitive self-representations. Through posited connectivity patterns, the activation in the PCC would then initiate greater activation in the IPL and MPFC. Activation within the IPL may guide the retrieval of prior self-knowledge and integrate the meaning of incoming information that may contribute to sense of self. IPL activation next influences the increase in MPFC activity which may aid the process of individuals' ability to discern whether incoming information is relevant to the self and potentially directs individuals' thought to internal sensory and/or emotional information. Finally, there may be regulatory effects that inhibit activation of the PCC from both the MPFC and IPL. Evidence shows that altered neural functioning in the same network of regions during self-referential processing plays a role in depression (Davey, Breakspear, Pujol, & Harrison, 2017; Lou, Lei, Mei, Leppänen, & Li, 2019). Specifically, depressed adults, compared to healthy adults, exhibited greater activation in the PCC during self-appraisal in addition to also showing a pattern of significantly stronger negative influence of the MPFC on the PCC (Davey et al., 2017). This pattern was suggested to indicate that there may be a hyper-regulatory influence from the MPFC on the PCC in depressed individuals, which could contribute to the enhanced self-focus found in those with depression (Davey et al., 2017; Whitfield-Gabrieli & Ford, 2012).

Neurocognitive models of self-referential processing and depression in adolescents have yet to be investigated using network analysis approaches; however, results of recent studies have begun to highlight the importance of examining self-referential neural processing in adolescence. Evidence shows that there is neural activation in adolescents within the same cortical midline structures found in adults, including the mPFC, the ACC, and the PCC/precuneus, during self-referential neural processing paradigms (review by Pfeifer & Peake, 2012). There is also evidence linking social-cognitive regions, including the TPJ and superior temporal cortex regions, to adolescent self-referential processing (Pfeifer & Peake, 2012). Studies have compared neural activation when adolescents are processing whether descriptive phrases are true about them to neural activation when adolescents are processing if the phrases are true of someone else or during an active control condition. These have shown that healthy adolescents exhibit activation during direct self-referential processing conditions in the medial PFC (including dorsal and ventral regions; BA8, BA9, BA10) and the ACC (BA24, BA32) (Debbané et al., 2017; Dégeilh et al., 2015; Jankowski, Moore, Merchant, Kahn, & Pfeifer, 2014; Pfeifer, Kahn, et al., 2013; Pfeifer, Merchant, et al., 2013; Romund et al., 2017; Schneider et al., 2012; Veroude, Jolles, Croiset, & Krabbendam, 2014). In addition, studies have also found activation in self-referential conditions in regions of the PCC/precuneus and posterior parietal cortex (BA23, BA31, BA7) (Debbané et al., 2017; Dégeilh et al., 2015; Jankowski et al., 2014; Romund et al., 2017; Schneider et al., 2012; Veroude et al., 2014). Although less consistent, activation during self-referential conditions has also been exhibited in superior and middle temporal cortex/TPJ regions (BA21, BA22, BA39) (Dégeilh et al., 2015; Romund et al., 2017).

Furthermore, research has shown that when compared to adults, children and adolescents actually activate self-referential processing regions to a greater extent when attending to self-relevant information and when feelings of self-consciousness are induced (Blakemore, den Ouden, Choudhury, & Frith, 2007; Burnett, Bird, Moll, Frith, & Blakemore, 2009; Pfeifer, Lieberman, & Dapretto, 2007; Pfeifer et al., 2009; Somerville et al., 2013). These findings suggest that information relevant to the self may be especially salient to adolescents, both subjectively and neurobiologically. Research conducted with early- to mid-adolescents (i.e., prior to age 15) may be particularly fruitful in elucidating the neurobiological mechanisms that could help explain how self-concept is associated with adolescent depression. Therefore, the overarching aim of this study was to investigate the relationship between neural self-referential processing and behaviorally reported levels of adolescent self-concept and the role these play in adolescent depression. Specifically, the current study tested whether there are particular functional neural patterns in the self-referential brain network during the processing of self-relevant information that make some youth more vulnerable to long-lasting, depressogenic effects of declines in self-concept found to begin in early adolescence. If found, such patterns of neural susceptibility for depressive symptoms during self-referential processing may be consequent to youths' histories of social interactions with parents, peers, or both, as proposed by the symbolic interactionist theory (Shrauger & Schoeneman, 1979).

To date, there are studies suggesting differences between how depressed and non-depressed adolescents process self-relevant information. Although many of these studies were not designed with the intention of assessing self-referential neural functioning, results have been found within the neural self-referential network. Three studies have reported results specific to self-referential neural processing of negative stimuli in depressed versus non-depressed adolescents. Two of these utilized explicit social feedback, including from parents (i.e., criticism) or peers (i.e., rejection), which found that adolescents with depression exhibit greater activation in self-referential regions, including the precuneus (BA7/31) and dACC (BA32/8), in response to negative social feedback, whereas healthy youth deactivated these regions and others, including the PCC and inferior parietal lobe/TPJ regions (BA39) (Silk et al., 2017; Silk et al., 2014). The third study found that compared to healthy youth, youth with remitted depression exhibited greater activation in self-referential regions (including the precuneus (BA7/31), middle and superior temporal gyrus (BA30, BA22), and ACC (BA24) while ruminating about situations in which they had felt the saddest, most frustrated, or like a failure (Burkhouse et al., 2017).

In addition, six studies have shown associations between neural processing of positive self-relevant information and depression in adolescents. Specifically, one study, in which adolescents specified whether positive trait adjectives were true about them, found that depressed adolescents showed greater activation, while healthy youth showed deactivation, in response to positive traits (relative to baseline) in the PCC/precuneus (BA23, BA30) (Bradley et al., 2016). Similarly, another study found that 10- to 12-year-old youth at high-risk for depression (based on maternal depression) exhibited greater activation in the VLPFC and vMPFC when self-evaluating on positive traits, compared to low-risk youth (Liu et al., 2019). Further, VLPFC activation mediated the relationship between maternal depression and depressive symptoms in youth, but only for youth who endorsed less positive self-traits. In response to peer acceptance stimuli, compared to a control condition, greater activation in the MPFC (BA10), precuneus (BA7/23/31), and superior temporal gyrus (BA39) were found in adolescents at high risk for depression (defined by maternal history of depression) compared to low-risk youth (Olino, Silk, Osterritter, & Forbes, 2015). However, high-risk adolescents in this study were also found to have lower activation than low-risk adolescents in the ACC (BA24/32) in response to peer acceptance (Olino et al., 2015). Findings from the remaining three studies suggest that depressed adolescents show less activation during the self-referential processing of positive stimuli. For instance, less activation was found within the dACC (BA9/32) in response to positive trait adjectives, compared to negative traits, in adolescents with depression (Quevedo, Ng, Scott, Smyda, et al., 2016). Similarly, depressed adolescents were also reported to exhibit lower activation in the vMPFC (BA10/11) and precuneus (BA7) when listening to maternal praise, relative to neutral statements; whereas healthy youth showed no differences between the two conditions (Silk et al., 2017). In the third study, depressed adolescents with high suicidality exhibited the lowest activation in response to their own happy facial expressions, relative to others' happy expressions, in the medial PFC (BA10), compared to depressed adolescents with low suicidality and healthy adolescents (Quevedo, Ng, Scott, Martin, et al., 2016).

Overall, evidence suggests that there are differences in neural self-referential processing between adolescents with and without depression. Given that depressed adolescents are presumed to have lower levels of self-concept, compared to healthy adolescents, these findings help to guide hypotheses, though indirectly, regarding how the adolescent brain processes self-relevant information under conditions of low versus high self-concept. Specifically, the evidence suggests that when processing negative self-relevant information, adolescents with depression exhibit greater neural activation in self-referential processing regions, compared to healthy adolescents. These results indicate that negative self-relevant information may be processed as more salient and relevant to the self in depressed adolescents, compared to non-depressed adolescents. With respect to neural self-referential processing of positive self-relevant information, the results were more mixed, pointing to several possible hypotheses on how adolescents with depression may be processing positive self-relevant information. For example, the results showing that depressed adolescents show greater activation in response to positive self-information could suggest that depressed adolescents have an overall sensitivity to self-related information regardless of valence, or that depressed adolescents need for more neural resources to process positive information. Alternatively, results from the other three studies showed depressed adolescents activate less to positive information, compared to healthy adolescents, which could indicate that positive information is less salient to the sense of self in adolescents with depression.

Unfortunately, evidence directly relating neural function during self-referential information processing to adolescents' subjective feelings of self-concept is limited. For example, within healthy adolescents, greater activation in the dlPFC, precuneus and anterior temporal pole/superior temporal gyrus during self-evaluation on *both* positive and negative trait adjectives was associated with adolescents' self-reported beliefs that they are not deserving of help or love from others—suggestive of lower social self-concept (Debbané et al., 2017). Similarly, greater PCC/precuneus activation while making self-judgments of personality traits across both valences was associated at a trend-level with less endorsement of positive traits and more endorsement of negative traits (effect sizes = -.28, .28, respectively) across healthy and depressed adolescents (Bradley et al., 2016). Findings from a third study reported that less dACC activation during self-referential processing of positive self-descriptors, compared to negative self-descriptors, was related to lower reported self-esteem and self-compassion across both healthy and depressed adolescents (Quevedo, Ng, Scott, Smyda, et al., 2016).

Findings of the first two studies demonstrate that activation in the PCC/precuneus region may not be sensitive to valence specific information; rather, it may be related to strength or salience of self-focused processing more broadly. If this is the case, the precuneus-behavior results reported in the first two studies may suggest that adolescents who have lower levels of positive self-regard may be especially vigilant or hyper-focused when thinking of their own attributes, as reflected by greater activation patterns in the PCC/precuneus. The third finding suggests that low self-esteem is associated with neural activation specifically when processing positively valenced information (i.e., less dACC activation to own *positive* traits). Although analyses do not specify whether activation in this contrast was driven by neural response to positive, negative, or both valences compared to a baseline or control condition, this result may suggest that the dACC region is particularly sensitive to valence-specific information. Although this region is found to be commonly activated during self-referential processing conditions, this interpretation would be consistent with other research implicating the dACC in processing the salience of affect (Eisenberger & Lieberman, 2004). Given the paucity of studies addressing direct associations between neural self-referential processing and adolescent-reported self-perceptions, conclusions on how high versus low self-concept is differentiated in the adolescent brain are, at best, preliminary. Beyond the three studies discussed above, currently, researchers are left to speculate that self-referential neural processes found within adolescents with depression are reflective of low self-concept. This is not particularly definitive, though, given that depression is a disorder defined by a cluster of symptoms and not solely by low self-concept or esteem. Therefore, the current study specifically tested whether there are patterns of neural function in brain regions implicated in self-referential processing that differentiate feelings of low self-concept in adolescents, which may subsequently help to predict increases in future depressive symptoms.

Given the previous research on how brain regions in the self-referential network act in concert during self-referential processing in adults and adolescents diagnosed with depression, the focus of the current study will be specific to the functioning of the MPFC, the ACC, the PCC/precuneus, IPL and TPJ regions. Because the research is limited, the current study aimed to clarify how behavioral reports of adolescent self-concept are associated with specific neural mechanisms related to self-referential processing. Based on the adult literature, it was hypothesized that self-referential regions in the brain would be hyperactive when adolescents were at-risk for depression due to low levels of self-concept. This study, therefore, helps to delineate the patterns of neural activation in self-referential processing regions that reflect negative and positive self-concept, and possibly improves our understanding of the etiology of depression. It has been posited from literature on the default mode network that deactivation of self-processing brain regions during goal-oriented tasks is a reflection of reduced self-focus processes, which in turn enables greater focus on non-self-relevant cognition (see review by Raichle et al., 2001). If so, the hyperactivation found in depressed adolescents to negative self-relevant information may be an indication that these adolescents may be less able to reallocate neural resources to other more cognitive or reappraisal processing necessary to adaptively cope. Such information would help to highlight a neurobiological risk factor for depression. More broadly, this information may guide our knowledge on the neurobiology of self-concept development and possibly highlight neural targets for intervention practices specific to adolescent depression. This type of information could be critical from both developmental and clinical perspectives.

1.2 The Current Study

The current study investigated how neural self-referential processing relates to adolescent self-concept reported through self-report and behavioral responses during a self-relevant trait adjective imaging task. Furthermore, the study examined whether neural patterns of self-referential processing confered risk for elevated depression through their relationship with behavioral reports of adolescent self-concept. This may be particularly important for elucidating the neurobiological underpinnings of the onset and maintenance of MDD. Specifically, the current study included early-adolescent girls (11-to-13-years old) recruited to range in risk for future depression, as a function of their levels of shy and fearful temperaments (Karevold, Røysamb, Ystrom, & Mathiesen, 2009). Adolescents reported on their level of self-concept using the Perceived Competence Scale for Children and Adolescents (Harter, 1982). This scale was created to assess youth's self-concept according to multidimensional theory of self-concept. Accordingly, self-concept is theorized to be a hierarchical construct in which regard for the self is distinct and variable for a variety of life domains (e.g., academic, social, physical, and athletic), and that these self-perceptions of domain-specific competencies help youth make inferences regarding a higher-order construct of general self-worth, also referred to as self-worth/esteem (Harter, 1982; Marsh & Shavelson, 1985). The current study specifically focused on adolescents' self-concept scores for the social and global domains, because there have been studies suggesting that these two domains are most related to adolescent depression (King et al., 1993; Marsh et al., 2004). Also, characteristics within these two domains are most similar to those utilized in the neuroimaging task.

Adolescents also participated in a functional neuroimaging (fMRI) assessment, during which they completed an imaging task designed specifically to compare self-referential processing to a control condition (adapted from Jankowski et al., 2014). Stimuli within this imaging task included self-descriptive traits spanning across social and physical self-competence and general worth domains. During the task, adolescents were asked to respond how true they believed each trait adjective was about them. The current study considered the following brain regions as part of the self-referential neural processing network: the MPFC (to include the dorsal/BA8 and 9; medial/BA10, and ventral/BA11 regions), the ACC (to include BA24 and BA32), the PCC (BA23, BA30), precuneus (BA7, BA31), the IPL (BA39, BA40), and TPJ (BA22) regions. The TPJ region was included because this region was frequently found to be activated during self-referential processing conditions, compared to other-person processing, in both healthy and depressed adolescents (Debbané et al., 2017; Olino et al., 2015; Romund et al., 2017; Saxbe, Del Piero, Immordino-Yang, Kaplan, & Margolin, 2015; Silk et al., 2017; Silk et al., 2014). This may be a developmental difference, as anterior regions are typically found more prominently in self-reflection in adults (Araujo et al., 2013). Given that adolescence is a period in which youth rely heavily on external cues from the social context to help define their own sense of self or identity (Harter, 1999; Rankin et al., 2004), neural activations found in the TPJ may reflect greater need for social-cognitive processes within posterior brain regions to help integrate external information as self-relevant, whereas in adults, this may no longer be necessary as self or one's identity has become more crystallized or automatized. Finally, both during the fMRI assessment and approximately 6 months later, youth also reported on their depressive symptoms.

The study investigated the following aims and related hypotheses:

AIM 1. To investigate whether neural self-referential processing relates to adolescents' perceptions of self-concept measured through the Perceived Competence

Scale (i.e., self-report) and behavioral responses during the fMRI self-referential processing task.

Hypothesis 1a: Lower reported levels of adolescent self-concept (measured through self-report and behavioral response during the scan) would be associated with greater neural activation in the self-referential network while processing negative self-relevant traits, compared to when processing positive self-relevant traits.

Hypothesis 1b: Lower reported levels of adolescent self-concept (measured through self-report and behavioral response during the scan) would be associated with lower neural activation while processing positive self-relevant traits, compared to when processing negative self-relevant traits.

AIM 2. To assess the associations between self-referential neural activation and adolescent reported depressive symptoms.

Hypothesis 2a: The same patterns of neural activation during self-referential processing hypothesized to be related to lower levels of self-concept (i.e., greater neural activation while processing negative traits and lower activation while processing positive traits) would be associated with higher levels of concurrent adolescent reported depressive symptoms.

Hypothesis 2b: The same patterns of neural activation during self-referential processing hypothesized to be related to lower levels of self-concept (i.e., greater neural activation while processing negative traits and lower activation while processing positive traits) would be associated with higher levels of adolescent reported depressive symptoms approximately 6 months later.

AIM 3. To test indirect effects models of neural self-referential processing and adolescent risk for depression (see Figure 1).

Hypothesis 3: Self-referential neural activation would be related to adolescent depressive symptoms through indirect relationships with all three measures of adolescent reported self-concept (assessed in individual models).

The overall aim of the study was to test an indirect effects model positing that brain function during self-referential processing would predict levels of adolescent depressive symptoms through its relationship with adolescents' behavioral reports of self-concept. The study was ideally positioned to test a risk model because it utilized a sample of adolescents that have no previous or current diagnosis of depression or anxiety and were specifically recruited to reflect a range from low-to-high risk for depression. However, it is important to note that there are most likely bi-directional effects between brain and behavior, which were not able to be fully disentangled in this study. Particularly, neural function and adolescent subjective perceptions of self were assessed within several weeks of each other, therefore directionality regarding this portion of the model was correlational. With regard to the relationship with adolescent depression, the study assessed depressive symptoms both concurrently and longitudinally. Therefore, hopefully this aspect of the model may help to further the field's understanding of directionality between low self-concept, its neural correlates, and risk for future depression.

Although limited, research has shown that both the affective salience and emotion regulatory networks play a role in processing and regulating response to threat and depression in adolescents. Even fewer studies to date have focused on understanding how parenting might affect the functioning of these networks during adolescence. Pertinent to the current study, only three studies to my knowledge have reported associations between parenting and adolescent neural response to threat in fronto-limbic regions (Elliott et al., Under Review; Guyer et al., 2015; Romund et al., 2016). Using a region of interest approach, one study found that greater adolescent-reported maternal warmth was associated with less amygdala reactivity in response to negative emotional faces, compared to neutral faces, in healthy 13-to-16 year old adolescents (Romund et al., 2016). The current study's sample of youth was drawn from a larger study on child anxiety treatment. Results from the larger study showed that when parents were observed using more positive socialization behaviors that encouraged youth to face challenges, healthy adolescents exhibited lower activation in the right anterior insula and perigenual cingulate (pgACC), while anxious adolescents showed higher bilateral anterior insula reactivity in response to threat words (Elliott et al., Under Review). The third study assessed the link between parenting and brain function using neural response specific to social threat in the Chatroom task (Guyer et al., 2015). Results showed that adolescents who exhibited a behaviorally inhibited (BI) temperament during infancy and toddlerhood had lower amygdala response to peer rejection, relative to acceptance, if they had mothers who reported higher levels of authoritative parenting, characterized by warmth, support, and involvement. In contrast, those adolescents who had mothers reporting higher levels of authoritarian parenting, characterized by harsh and punitive behaviors, showed lower VLPFC response to peer rejection, relative to baseline. These studies suggest that healthy adolescents show less threat-related affective salience activation to negative stimuli when they have warmer and more supportive parents. Findings from these studies are less clear regarding the emotion regulatory network, as regulatory neural network activations were shown to be lower in both healthy adolescents with parents who had harsher parenting styles and in healthy adolescents who had parents who used positive coping socialization practices. Mixed results could be due to the differences in measures of parenting (i.e. self-report vs. observations), in task stimuli, or the limitations of the task designs in their ability to directly test emotion regulation. Broadly, however, these studies support that adolescents may still be susceptible to or dependent on the influence of parenting socialization behaviors for the neurodevelopment of emotion processing network function, although this has not been tested in a prospective, longitudinal study.

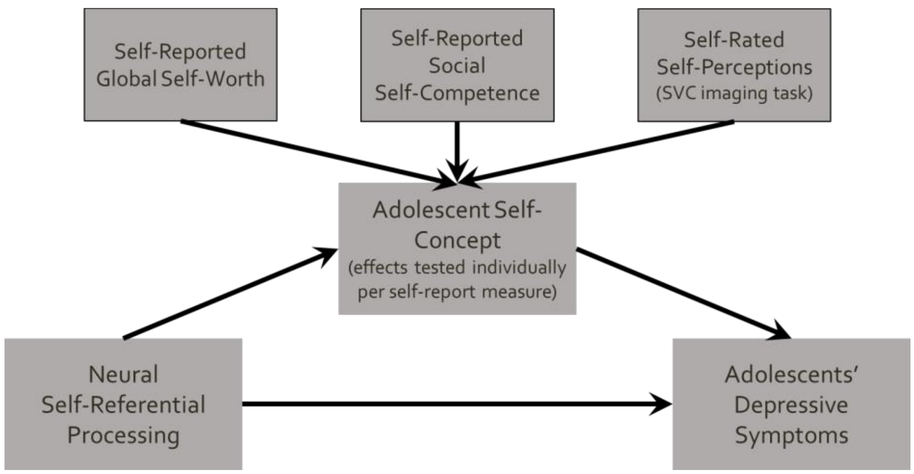

Figure 1. Proposed indirect effects model of neural self-referential processing and adolescent risk for depression.

2.0 Method

2.1 Participants

The present study includes a subsample of 11-to-13-year-old girls (*N*=48; M_{years}=12.19, *SD*=.80) from the GIRLS Brain Study (PI's: Silk and Ladouceur), a longitudinal study examining how neural sensitivity to social threats and rewards in the environment in shy and fearful early-adolescent girls may contribute to the development of social anxiety and depression. Participants were initially recruited for the GIRLS Brain Study based on parent- or child-reported levels of temperamental risk assessed using the Fear and Shyness subscales of the Early Adolescent Temperament Questionnaire-Revised (Ellis & Rothbart, 2001). They were recruited from the community through local media advertisements, referrals from pediatricians, targeted mailings, research registries, and other University research studies. Once enrolled in the GIRLS Brain Study, participants were recruited for the supplement study at their second laboratory visit by research assistants.

As in the GIRLS Brain Study, adolescents were excluded if they met criteria for a current or past DSM-5 diagnosis of Anxiety Disorder (except specific phobia) or major depressive disorder. Exclusion criteria also included an IQ < 80, as assessed using the Wechsler Abbreviated Scale of Intelligence (WASI), lifetime presence of a neurological or serious medical condition, lifetime presence of a DSM-5 Psychotic or Autistic Spectrum Disorder, presence of MRI contraindications (e.g., dental braces, history of metallic foreign objects in body such as aneurysm clips or other devices or questionable history of metallic fragments, claustrophobia), uncorrected visual disturbance (<20/40 Snellen visual acuity), left handedness, presence of head injury or congenital neurological anomalies (based on parent report), taking medications that affect the central nervous system and endocrine function (e.g., SSRI's, oral steroids, oral contraceptives), being acutely suicidal or at risk for harm to self or others. Stimulant medications were permitted, if not required for 36 hours before the scan. The GIRLS Brain Supplement: Self-Processing in the Adolescent Brain Study was approved by the University of Pittsburgh Institutional Review Board and written informed consent and assent were obtained from participating primary caregivers and adolescents.

2.2 Procedure

Prior to enrollment in the current study, participants were required to have completed all screening procedures, met inclusionary criteria, and be enrolled in the GIRLS Brain study. As part of the GIRLS Brain Study, participants completed clinical interviews, laboratory interaction tasks, functional neuroimaging visits, and questionnaires, including adolescent-reports of self-concept and depressive symptoms (relevant for the current study). At the second GIRLS Brain laboratory visit, participants and their parents received a full explanation of all aspects of the current study protocol and procedures, and parents and adolescents completed consent/assent. Following the initial GIRLS Brain functional neuroimaging (fMRI) assessment (i.e., 3^{rd} GIRLS Brain study visit), consented participants were scheduled to complete an additional fMRI visit within approximately 4-to-8 weeks for the current study.

Participants and their primary caregivers were asked to complete a 1.5 hour visit for the current study at the MR Research Center in the UPMC Presbyterian Hospital, Pittsburgh, PA, several weeks following their initial visit for the larger study. At this visit (timepoint 1; T1), primary caregivers and youth completed questionnaires, including adolescent-reports and parent-reports of adolescents' anxiety and depressive symptomatology. Next, adolescents practiced in a simulator to become as familiar and comfortable as possible with the scanner environment and imaging task protocol. Following the practice session, adolescents completed a 30-minute fMRI scanning session. As part of the one-year follow-up protocol for the larger GIRLS Brain Study, girls completed self-report questionnaires on depressive symptoms which were used as an outcome measure for the longitudinal timepoint (T2) in the current study. This T2 timepoint was approximately 6 months (*M*=6.37, *SD*=1.46) following T1 (i.e., the initial supplement study visit). Nine adolescent girls were excluded from study analyses due to excessive fMRI motion artifacts (see fMRI Data Analysis section) and an additional participant was excluded from longitudinal analyses, due to missing follow-up data. Therefore, a total of 39 participants are included in all analyses and 38 are included in longitudinal analyses. See Table 1 for final sample characteristics.

Table 1. Adolescent girls' demographics at time of scan (T1).

N=39	*M* (*SD*)	Range
Age	12.27 (.80)	11-13
Race [n (%)]		
White, non-Hispanic	24 (61.5)	
Black	9 (23.1)	
Bi-racial	4 (10.3)	
Asian	1 (2.6)	
Native American	1 (2.6)	
Head of Household Education [n (%)]		
High school graduate	4 (10.3)	
Some college	10 (25.6)	
College degree	7 (17.9)	
Graduate training	18 (46.2)	
Pubertal Status	3.54 (1.19)	1.00-5.00
Self-reported SES[1]		
Family status within society	7.03 (1.55)	4.00-10.00
Self-Concept Measures		
Global Self-Worth	3.37 (.46)	2.42-4.00
Social Self-Competence	2.95 (.69)	1.17-4.00
In-Vivo Self-Perception Ratings	146.44 (12.60)	120.00-172.00
T1 Depressive Symptoms [M(SD)]	5.82 (4.51)	0.00-15.00
T2 Depressive Symptoms [M(SD)][2]	9.20 (7.88)	0.00-30.50

[1]SES=Socioeconomic Status, [2]T2 depressive symptoms based on data from 38 participants.

2.3 Measures

2.3.1 Self-Perception Profile for Children (Harter, 1982, 1985)

The Self-Perception Profile for Children is a 36-item self-report questionnaire that assesses sense of self-competence across several domains in youth 8 to 13 years of age. Self-competence for the following six domain subscales is assessed, using six items per subscale: academic, social, physical appearance, athletic, behavioral conduct, and global self-worth. The current study focuses on the social self-competence and global worth subscales. For each item, participants are provided with two alternative statements regarding how they might view themselves in a domain. They are asked to choose which of the two statements most closely reflects their self-perception and are then prompted to respond whether that statement is “sort of true for me” or “really true for me”. Examples of statements include: “Some kids wish that more people their age like them BUT Other kids feel that most people their age do like them” (social); “Some kids find it hard to make friends BUT Other kids find it’s pretty easy to make friends” (social); “Some kids would like to have a lot more friends BUT Other kids have as many friends as they want” (social); “Some kids like the kind of person they are BUT Other kids often wish they were someone else” (global); “Some kids are often unhappy with themselves BUT Other kids are pretty pleased with themselves” (global). A score of 1 (lowest perceived competence) to 4 (highest perceived competence) is possible on each item. The mean score for each subscale reflects the youth’s sense of self-competence within each domain separately. The current study will focus on the social self-concept and global self-worth subscales, for which reliability in the current sample was high (α=.80 and .84, respectively).

2.3.2 Mood and Feelings Questionnaire (MFQ-C), Child-Report

The Mood and Feelings Questionnaire (MFQ; Costello & Angold, 1988) is a 33-item self-report questionnaire assessing depressive symptoms in youth 8 to 18 years of age. Participants are asked to rate how true each item is of their mood and behavior within the past two-weeks on a three-point Likert scale (0 = “not true,” 1 = “sometimes,” 2 = “true”). Sample items include “I felt miserable or unhappy,” “I cried a lot,” “I slept a lot more than usual.” The MFQ is administered at various points throughout the larger GIRLS Brain Study. Adolescent-reported, total scores from two timepoints were used for the current study, including time of the supplement study scan (T1) and approximately 6 months (M=6.37, SD=1.46) later at participants’ GIRLS Brain Study one-year follow-up (T2). Adolescent-reported total scores from both timepoints were used as outcome measures. Higher total scores reflect greater symptomatology. Reliability for the MFQ in the current sample was high (α=.90) at both timepoints.

2.3.3 Pubertal Development Scale (PDS)

The Pubertal Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988) is a five item self-report that assesses physical development associated with pubertal changes. The current study used an adapted coding system (Shirtcliff, Dahl, & Pollak, 2009) that captures gonadal and adrenal hormonal signals of physical development on a 5-point scale. Pubic⁄body hair and skin changes were assessed in girls, as they are associated with adrenal hormones. Gonadal hormonal signals in girls are measured using questions about growth spurt, breast development, and menarche. Total score (ranging 1-5) from the PDS was used as covariate in the current study analyses. Reliability for the PDS in the current sample was high (α=.74).

2.3.4 Macarthur Scale of Subjective Social Status-Youth Version (Goodman et al., 2001)

This scale assesses adolescents' subjective feelings of socioeconomic and social status with respect to both the broader, American society and the more proximal social environment of adolescents' school environment. The current study uses only adolescents' assessments of their socioeconomic status (SES) in study analyses as a covariate. For this measure, adolescents are given a picture of a ladder and asked to "imagine that the ladder pictures how American Society is set up. At the top of the ladder are people who are the best off-they have the most money, highest amount of schooling, and the jobs that bring the most respect. At the bottom are people who are the worst off. They have the least money, little or no education, no job or jobs that no one wants or respects." Adolescents are then asked to think about their family and to rate where they believe their family would be on the ladder, "worst off (1)" to "best off (10)". Adolescents' subjective perceptions of SES were not significantly correlated with parents' reports of head of household education (r=.063, p=.89) or family income level (r=-.127, p=.45). However, it has been shown that subjective measures of family SES are more predictive of psychological attributes, including self-esteem, in adolescents and adults, compared to objective measures (Adler, Epel, Castellazzo, & Ickovics, 2000; Chen & Paterson, 2006). Therefore, this measure was chosen to use as a covariate in the current study analyses.

2.4 Functional Magnetic Resonance Imaging

2.4.1 Self-Versus-Change Task (SVC; Adapted from Jankowski et al., 2014)

Participants were presented with trait adjective words that are associated with positively- (n=27) and negatively-valenced (n=23) personality characteristics. The trait adjectives are representative of prosocial, insecure, and aggressive characteristics encompassing social, physical, and global aspects of self. Examples of words include: “friendly,” “trustworthy,” “boring,” “pushover,” “depressed,” “selfish,” “rude,” and “ugly.” During the task, participants are presented with each of the 50 trait adjective words twice, once during a self-evaluative condition in which adolescents respond whether the traits are true about themselves and once during a malleability-evaluative (i.e., change) condition in which adolescents respond whether the trait can change in people (generally) during their lives.

The imaging task is a mixed block/event-related design which includes 20 blocks total, 10 blocks of two types (self-evaluative and change conditions). During the self-evaluative block type, participants are instructed to rate how true the trait adjective is about them on a 4-item Likert scale (1=“not at all,” 2=“a little,” 3=“mostly,” or 4=“definitely”). During the change condition, which serves as an active control, participants are asked how much the trait adjectives can change in people (generally) during their lives, using the same 4-point Likert scale response options. Both positive and negative trait adjective trials are included within each block. Stimuli are presented using E-Prime software (Psychology Software Tools, Pittsburgh, PA) and behavioral responses are collected using a Psychology Software Tools™ glove. Each block (31.3 seconds) begins with a brief instruction screen (3000ms), followed by five trait adjective events (4500ms/event), each separated by a preset jittered interstimulus interval (ISI; *M*=277.25ms). Following the final event in each block, a 4500ms rest interval (blank screen) occurs. Two versions of the task were created, one in which the task begins with a self-evaluative block type and the second in which the task begins with a malleability-evaluative block type. Participants were randomly assigned to task versions, for an even distribution. Participants were trained on the paradigm during a simulator session prior to the scan.

Following the scanning session, participants completed a post-task valence identification worksheet following their scan session, on which they circled whether they considered each of the 50 trait words to be a “positive (good) or negative (bad/not so good) way to be described.” The post-task valence identification worksheet was added to the study protocol approximately halfway through the study; therefore, ratings were completed by only 20 study participants. Trait words that did not meet an 80% confirmation rate on valence were not included in the final “In-Vivo Self-Perceptions” variable used for study analyses. Accordingly, four traits received mixed ratings. Specifically, participant ratings indicated mixed ratings on valence for “shy” (50% negative rating), “flirty” (60% positive rating), “risky” (60% negative rating), and “assertive” (55% positive rating) trait words. Therefore, these four traits were excluded from use in the final analyses. The In-Vivo Self-Perceptions variable was created using participant self-perception ratings on the remaining 21 negative and 25 positive trait words which had been presented during the self-evaluative condition of the SVC task. Ratings of negative trait words were reverse coded, such that higher ratings indicated less negative self-perceptions, and summed with ratings of positive trait words for each participant. Using this sum total, the In-Vivo Self-Perception variable could range from 46 (most negative possible self-perception rating score) to 184 (most positive possible self-perception rating score).

2.4.2 Imaging Acquisition and Preprocessing

2.4.2.1 Data Acquisition

Multiband images were acquired on a 3T Siemens Trio scanner. Stimuli were projected using a color high resolution LCD projector. Each volume consisted of 60 slices (3.2mm thick). Volumes were acquired parallel to the anterior-posterior commissure line using a T2*-weighted echo planar imaging pulse sequence with 15000ms repetition time (TR), 30ms echo time (TE), 55° flip angle, 3.2 x 3.2 x 3.2mm voxels, 220 x 220 field of view (FOV), 96 x 96 matrix size. Scanning began on the instruction screen of the first block. Approximately 21 volumes (2 during instruction screen; 3 per trial (x5); 3 during rest interval) were acquired per each of the 20 blocks. Therefore, a total of 150 volumes were collected for each block condition (self and change). 419 volumes were acquired throughout the entire 10.5-minute task. 192 high-resolution, T1-weighted MPRAGE images were also acquired (TR=2300ms, TE=3.93ms, TI=900ms, FOV=256 x 256, voxel size=1.0 x 1.0 x 1.0mm, flip angle=9°, slice thickness=1mm) for co-registration pre-processing procedures.

2.4.2.2 Data Analysis

Images were pre-processed using SPM12 (http://www.fil.ion.ucl.ac.uk/spm). Volumes were oriented to the AC-PC line and realigned to correct for head motion. Images were segmented and co-registered to the first functional image. Realigned images were spatially normalized to a standard MNI template (Montreal Neurological Institute template) using a 4th degree B-spline interpolation method. Normalized images were smoothed with a 6mm full-width at half-maximum Gaussian filter. Voxels were resampled to be 2mm^3. If participants exhibited absolute motion greater than 2mm/2º and global intensities more than 3 SD from the mean for more than 25% of volumes, they were excluded from analyses (*n*=9). Six motion parameters were included as regressors in the 1st level GLM design to correct for slow-drift motion.

The 1st level GLM model included a total of 11 regressors in the design. Four conditions were modeled, including self-positive, self-negative, change-positive, and change-negative, representing conditions in which participants are responding to positive versus negative trait adjectives either during the self or change condition types. Additionally, the rest interval and six motion parameters were modelled in the 1st level design. A Self-Negative>Self-Positive contrast were created in the 1st level SPM design for the study analyses.

Whole-brain analyses were conducted within the group level design of SPM12. All results were conducted at an uncorrected, voxelwise, $p_{-uncorr}<.005$ threshold. Resulting cluster-wise activation that passed the family-wise, cluster-level error correction ($p_{-FWE}< .05$) in SPM were considered significant. If resulting clusters of activation that passed the family-wise error correction revealed especially large clusters spanning across multiple brain regions, then analyses were more conservatively thresholded at uncorrected, voxelwise, $p_{-uncor} <.001$, with family-wise, cluster-level error correction ($p_{-FWE}<.05$). Additionally, using a priori regions-of-interest (ROI) within the self-referential neural network, a single, self-referential network mask was created. Included ROIs for the mask were anatomically defined in the WFU PickAtlas Toolbox (v3.0.5), along with any additional functionally defined regions indicated by the "self" mask in Neurosynth. The self-referential mask included: the dmPFC (BA8/9), MPFC (BA10), vmPFC (BA11), the ACC (BA24 and BA32), the PCC/precuneus (BA23, BA7, and BA31), the IPL (BA39/40), and TPJ (BA22). Using this mask, restricted whole-brain analyses were also conducted to assess whether significant results were within hypothesized regions.

3.0 Data Analytic Plan

All measures to be included as independent variables in analyses were assessed for outliers. Outlying data points were winsorized to 25th%ile /75th%ile +/- 1.5xIQR.

To assess Aim 1, regression analyses were completed at the 2nd level in SPM12. Three analyses were conducted, each including one of the three adolescent-reported measures of self-concept (i.e., global self-worth, social self-competence, and In-vivo self-perceptions; lower scores = more negative self-concept) as a regressor on brain activation using the Self-Negative>Self-Positive contrast. T-tests assessed positive (testing Hypothesis 1a) and negative (testing Hypothesis 1b) correlations between neural activation and adolescents' scores of self-concept. Significant results were further probed to explore effects of covariates and to assess which condition was driving significant effects. To explore effects of covariates, MarsBar was used to extract parameter estimates of activation during the Self-Negative>Self-Positive contrast for any resulting significant cluster. Models using the Process macro in SPSS were used to explore main effects of covariates and brain activation X covariate interaction effects on levels of self-concept.

To assess Aim 2, again, regression analyses were conducted at the 2nd level in SPM12 to measure associations between neural activation and adolescent depressive symptoms. For Hypothesis 2a, a regression analysis was conducted to assess the hypothesis that there would be positive correlations between the Self-Negative > Self-Positive contrast and adolescents' self-reported depressive symptoms at the time of the scanning session (T1) (higher MFQ score = greater depression). The same approach was used for Hypothesis 2b, however, using adolescents' self-reported depressive symptoms at T2 (approximately 6 months following the scanning session) as a regressor within the models, while controlling for T1 depression scores. Using the same posthoc analysis approaches described for Aim 1, significant results were probed to explore effects of covariates.

To test Aim 3, a within-sample t-test was completed in SPM12 to measure significant neural activation that was positively and negatively correlated with the Self-Negative > Self-Positive contrast. Parameter estimates from resulting clusters that passed cluster-wise corrections were extracted for each participant. Indirect effects were tested in SPSS using the PROCESS macro. Extracted neural activation values for each significant cluster were entered as independent variables in separate models; adolescent self-concept values were entered as mediating variables in separate models for each measure of self-concept; and adolescent depression scores were the dependent variables. Indirect effects were assessed for concurrent depression and for longitudinal depressive symptoms in separate models.

Although the age range of the sample was designed to be restricted to 2 years (age 11 to 13 years), age was included as a covariate because levels of self-concept have been known to be variable during highly transitional periods, such as early adolescence (Cole et al., 2001). Research has also shown that neural activation to self-relevant stimuli increases with age during adolescence (Burnett et al., 2009; Dégeilh et al., 2015; Guyer, Choate, Pine, & Nelson, 2012; Pfeifer, Kahn, et al., 2013). Furthermore, the sample age range was chosen to include variability in pubertal status. Therefore, pubertal status was also included as a covariate. Behavioral research has also found evidence for possible effects of socioeconomic status (SES) on adolescent self-concept; however, these have been limited and mixed. For example, one study has shown that adolescents in higher SES contexts have lower self-esteem than adolescents from middle-class environments (Richman, Clark, & Brown, 1985), whereas a more recent meta-analysis found that there is a small, but positive relationship between SES and self-esteem (i.e., higher SES is related to higher self-esteem) within school-age and adolescent samples (Twenge & Campbell, 2002). In addition, SES has been associated with neural factors, including structural and functional differences in regions that support self-referential processing such as the PFC and ACC (Gianaros et al., 2007; McEwen & Gianaros, 2010). Therefore, SES was also included as a covariate in analyses using the SES subscale of the Macarthur Scale of Subjective Social Status-youth version. Moderating effects of covariates on the proposed models were explored, although power may have been insufficient to detect small effect sizes.

4.0 Results

4.1 Preliminary Results

Bivariate correlation analyses showed no significant associations between adolescent gender, T2 age, or T2 pubertal status and adolescent depressive symptoms at T3 (see Table 2 for associations). The sample of participants included only two non-White adolescents, therefore associations with race were not considered. T-tests showed no difference in T3 depressive symptoms between adolescents who completed CBT versus CCT anxiety treatments (t=.614, p=.542). Although no group differences were found between adolescents who completed the two therapy types in the current subsample, we previously found that treatment response predicted depressive symptoms in the CBT group, but not in the CCT group (Silk et al., Under Review), therefore therapy type (CBT vs. CCT) was included in all analyses as a covariate. Due to missing parenting data at T1 (observation data, n=10; self-report data, n=16) and/or missing T3 depressive symptom data (n=3), final model analyses will include subsamples of participants with full information available. Forty-four participants had available T3 depressive symptom assessments (i.e. 2.5-, 3.0-, or 3.5-year follow-ups). T3 depressive symptom outcomes were assessed approximately one year after the T2 fMRI assessment (M=12.53 months, SD=2.84). Models using observation data included 37 participants, and models using adolescent-report data included 31 participants.

4.1.1 Behavioral Data Associations

Bivariate correlation analyses were completed among the behavioral variables of interest and covariates, including adolescents' age, pubertal status, and socioeconomic status (SES) (Table 2). Adolescents' age was significantly correlated with pubertal status (r=.339, p=.04). Neither age nor pubertal status were significantly correlated with any other behavioral variable of interest. Adolescents' subjective report of SES was significantly associated with all three measures of self-concept, including global self-worth (r=.344, p=.03), social self-competence(r=.378, p=.02), and in-vivo self-perception ratings (r=.371, p=.02). Global self-worth was significantly correlated with social self-competence (r=.497, p=.001) and SVC self-perceptions (r=.584, p<.001); however, social self-competence and in-vivo self-perceptions were not significantly correlated (r=.238, p=.15). All three measures of self-concept were significantly and negatively associated with T1 and T2 depressive symptoms (ps<.05), with the exception of social self-competence and T2 depressive symptoms (p=.36). Depressive symptoms at T1 and T2 were highly correlated (r=.671, p<.001), and a paired-sample t-test showed that adolescents had significantly higher depressive symptoms at T2, compared to T1 (t=-3.773, p<.001).

Table 2. Correlations between participant demographics and behavioral variables of interest (N=39).

		1.	2.	3.	4.	5.	6.	7.	8.
1.	Age	1							
2.	Pubertal status	.339*	1						
3.	SES	.063	-.179	1					
4.	Global self-worth	.103	-.040	.344*	1				
5.	Social self-competence	.150	-.028	.378*	.497***	1			
6.	In-Vivo self-perceptions	-.145	-.057	.371*	.584***	.238	1		
7.	T1 Depressive Sx	.192	.193	-.245	-.345*	-.332*	-.495***	1	
8.	T2 Depressive Sx[1]	.018	.110	$-.290^{t}$	-.478***	-.151	-.495***	.671***	1

*$t<.10$*$p\leq.05$, **$p\leq.01$, ***$p\leq.005$; [1]Correlations with T2 depressive symptoms based off of 38 participants; Note: SES=Socioeconomic status, Sx=Symptoms.

4.1.2 Self-Negative vs. Self-Positive Activation

Results of a whole-brain, within-sample, t-test showed significant activation during the Self-Negative, relative to Self-Positive, condition in several regions ($p_{\text{-}uncorr}<.001$ voxelwise threshold) across all participants. Clusters that passed familywise error correction ($p_{\text{-}FWE}<.05$) were found in the left hemisphere and within the medial prefrontal cortex (MPFC), ventrolateral prefrontal cortex (VLPFC), supplementary motor area/dorsal medial prefrontal cortex (SMA/dMPFC), and left visual association area regions. Using the same thresholds, one cluster in the right visual association area was found to be associated with greater activation during the Self-Positive, relative to Self-Negative, condition (Table 3; Figure 2). None of these results held using the originally proposed self-referential processing mask. All findings reported below are, therefore, results of whole-brain analyses.

Table 3. Whole-brain, within-sample, t-test results comparing Self-Negative and Self-Positive conditions ($p_{\text{-uncorr}}$<.001 voxelwise threshold; $p_{\text{-fwe}}$<.05 clusterwise threshold).

				Peak Voxel Coordinates				
	Hem.	*Region*	*Brodmann Area*	*x*	*Y*	*Z*	*k*	*t-statistic (df=38)*
Self-Negative > Self-Positive								
	L	VLPFC	45/47	-50	20	14	990	5.62
	L	dMPFC	8	-8	44	48	140	5.03
	L	SMA/dMPFC	6/8	-10	20	60	184	4.60
	L	Visual association	18	-22	-100	6	737	6.90
Self-Positive > Self-Negative								
	R	Visual association	18	20	-92	12	198	5.87

Note: R=right, L=left; VLPFC=ventrolateral prefrontal cortex; dMPFC=dorsal medial prefrontal cortex; SMA/dMPFC=supplementary motor area/dorsal medial prefrontal cortex.

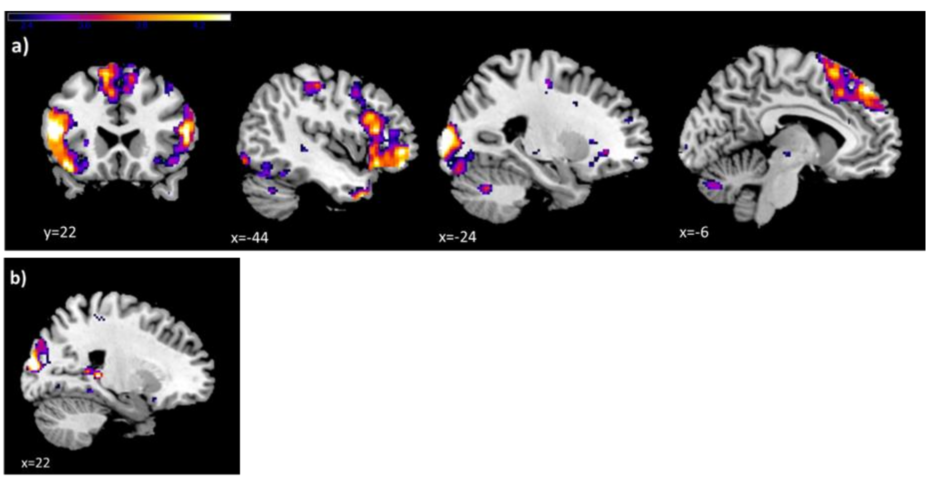

Figure 2. Whole-brain activation during a) Self-Negative>Self-Positive condition and b) during Self-Positive>Self-Negative condition ($p_{\text{-uncorr}}$<.001 voxelwise threshold; $p_{\text{-fwe}}$<.05 clusterwise threshold).

4.2 Primary Analyses

The total effect models showed that neither T1 observed nor adolescent-reported parental warmth significantly predicted adolescent depressive symptoms at T3 (β=-.249, *B*=-30.920 (*SE*=20.694), *p*=.144; β=-.228, *B*=-.545 (*SE*=.441), *p*=.227).

4.2.1 Aim 1

To investigate whether neural self-referential processing relates to adolescents' perceptions of self-concept measured through the Perceived Competence Scale (i.e., self-report) and behavioral responses during the fMRI self-referential processing task.

4.2.1.1 Global Self-Worth

Brain activation ($p_{\text{-}uncorr}$<.005 voxelwise, $p_{\text{-}FWE}$<.05 cluster threshold) was not significantly associated (positively or negatively) with adolescents' reports of global self-worth, using either a whole-brain analysis or the mask of self-referential processing regions.

4.2.1.2 Social Self-Competence

Adolescents' whole-brain brain activation was associated with their reports of social self-competence in several clusters across the whole brain ($p_{\text{-}uncorr}$<.001 voxelwise, $p_{\text{-}FWE}$<.05 cluster threshold; Table 4, Figures 3 & 4). Higher social self-competence was correlated with greater activation during the Self-Negative condition, relative to Self-Positive in the right posterior cingulate/precuneus (PCC/precuneus), right superior temporal gyrus/temporoparietal junction (STG/TPJ), left inferior parietal lobe (IPL), left visual cortex/IPL, and left cerebellum. When results were masked with the a priori, self-referential mask (voxelwise, $p_{-uncorr}$<.005; cluster-extent threshold, p_{-FWE}<.05), activation within the precuneus cluster remained significant. Parameter estimates of activation for each cluster were extracted and used in individual regression analyses to measure potential effects of covariates on social self-competence. In addition to brain activation, a main effect of SES was found to predict social self-competence across all models; however, no brain activation X SES interaction effect was found. Higher SES was associated with higher social self-competence (*Bs*=.120-.168, *ps*<.05). No main or interaction effects were found with age (*ps*>.22) or pubertal status (*ps*>.26).

Table 4. Whole-brain associations between self-negative>self-positive neural activation and greater social self-competence ($p_{-uncorr}$<.001 voxelwise threshold; p_{-fwe}<.05 clusterwise threshold).

				Peak Voxel Coordinates				
	Hem.	*Region*	*Brodmann Area*	*x*	*Y*	*Z*	*k*	*t-statistic (df=37)*
Self-Negative > Self-Positive								
	R	PCC/precuneus[1]	31/7	18	-52	44	1027	4.48
	R	STG/TPJ	21/22	50	-38	2	144	5.80
	L	IPL	39	-54	-54	32	152	5.41
	L	Visual cortex/IPL	19/39	-34	-72	12	136	4.54
	L	Cerebellum		-24	-84	-26	239	5.38
Self-Positive > Self-Negative (n/s)								

Note: R=right, L=left; PCC=posterior cingulate cortex; STG/TPJ=superior temporal gyrus/temporal parietal junction; IPL=inferior parietal cortex.[1]Similar region was found to have significant activation when results were masked with the a priori, self-referential mask (peak=18, -78, 44, k=894; voxelwise, p_{uncorr}<.005; cluster-extent threshold, p_{-FWE}<.05).

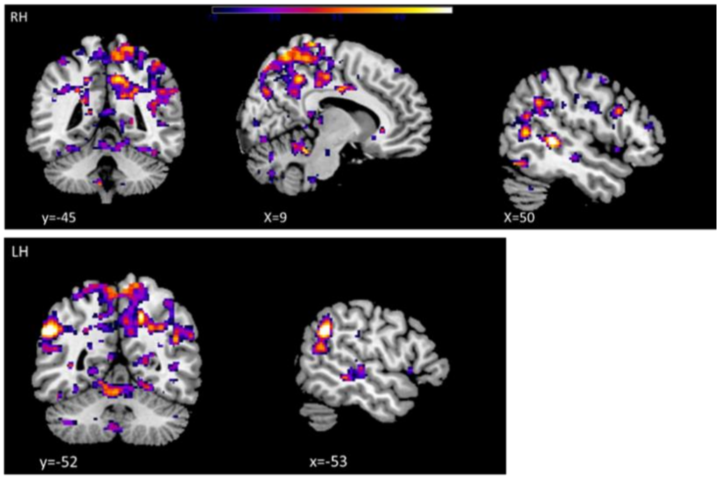

Figure 3. Higher social self-competence associated with greater activation during Self-Negative, relative to Self-Positive, condition (*$p_{\text{-}uncorr}$*<.001 voxelwise threshold; *$p_{\text{-}fwe}$*<.05 clusterwise threshold).

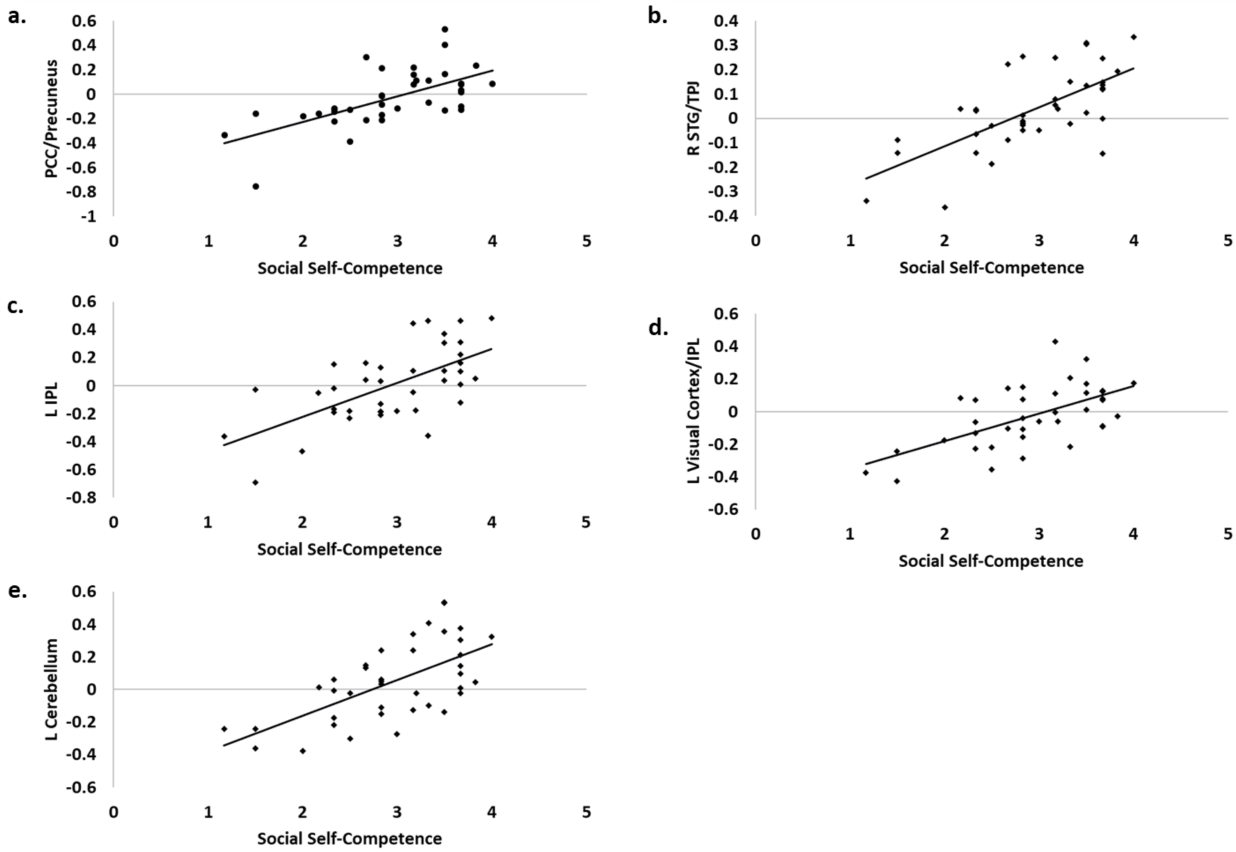

Figure 4. Relationships between adolescents' reports of social self-competence and neural response from Self-Negative>Self-Positive contrast in the: a) right posterior parietal cortex/precuneus; b); right superior temporal gyrus/temporoparietal junction; c) left inferior parietal lobe (IPL); d) left visual cortex/IPL; e) left cerebellum. Note: Average brain activation parameter estimates extracted from regression results using $p_{\text{-uncorr}}<.001$ voxelwise, $p_{\text{-fwe}}<.05$ clusterwise thresholds; L=left, R=right; positive numbers reflect more activation during self-negative condition, negative numbers reflect more activation during self-positive condition.

4.2.1.3 In-Vivo Self-Perception Ratings

Adolescents' whole-brain brain activation was associated with their reports of self-perceptions during the SVC fMRI task in one cluster ($p_{\text{-uncorr}}$<.005 voxelwise, $p_{\text{-FWE}}$<.05 cluster threshold); however, no significant results were found when using the self-referential processing mask. More positive in-vivo self-perception ratings were associated with greater neural activation during the Self-Positive condition, relative to Self-Negative, in the right visual association area (Table 5, Figure 5). Parameter estimates of activation for this cluster were extracted and used in individual regression analyses to measure potential effects of covariates on in-vivo self-perceptions. In addition to brain activation, a main effect of SES was found to predict in-vivo self-perceptions; however, no brain activation X SES interaction effect was found. Higher SES was associated with higher in-vivo self-perceptions (*B*=2.861, SE=1.08, *p*=.01). No main or interaction effects were found with age (*ps*>.69) or pubertal status (*ps*>.47).

Table 5. Whole-brain associations between self-positive>self-negative neural activation and greater in-vivo self-perception ratings ($p_{\text{-uncorr}}$<.005 voxelwise threshold; $p_{\text{-fwe}}$<.05 clusterwise threshold).

				Peak Voxel Coordinates				
	Hem.	*Region*	*Brodmann Area*	*x*	*Y*	*Z*	*k*	*t-statistic (df=35)*
Self-Negative > Self-Positive (n/s)								
Self-Positive > Self-Negative								
Main effect of Self-Perceptions								
	R	Visual association	18	16	-84	-4	352	4.58

Note: R=right.

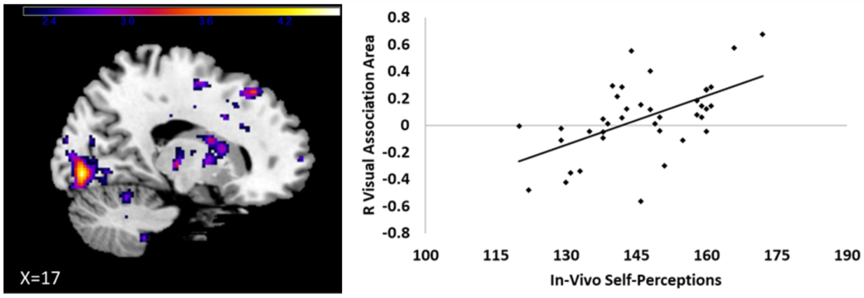

Figure 5. Relationship between adolescents' in-vivo self-perceptions and neural response from Self-Positive>Self-Negative contrast in the in the right visual association area. Note: Average brain activation parameter estimates extracted from regression results using $p_{-uncorr}$<.005 voxelwise, p_{-fwe}<.05 clusterwise thresholds; R=right; positive numbers reflect more activation during self-positive condition, negative numbers reflect more activation during self-negative condition.

4.2.2 Aim 2

To assess the associations between self-referential neural activation and adolescent reported depressive symptoms at time of scan (T1) and approximately six months later (T2).

4.2.2.1 T1 Depressive Symptoms

Significant associations were found between adolescents' brain activation and adolescents' reports of depressive symptoms in several clusters across the whole brain ($p_{-uncorr}$<.001 voxelwise, p_{-FWE}<.05 cluster threshold); however, no significant results were found using the self-referential processing mask. Higher levels of depressive symptoms were associated with greater activation during the Self-Negative, relative to Self-Positive, condition in the bilateral caudate/putamen, bilateral dorsal anterior cingulate/supplementary motor area (dACC/SMA), left somatosensory cortex/inferior parietal cortex (S1/IPL), and right medial visual association area (Table 6, Figures 6 & 7). Parameter estimates of activation for each cluster were extracted and used in individual regression analyses to measure potential effects of covariates on T1 depressive symptoms. In addition to brain activation within the visual association cluster, a main effect of SES was found to predict T1 depressive symptoms (B=-.917, SE=.369, p=.02); however, no brain activation X SES interaction effect was found. No main or interaction effects were found with age (ps>.16) or pubertal status (ps>.17). No correlations were found between brain activation to Self-Positive>Self-Negative and T1 depressive symptoms.

Table 6. Whole-brain associations between self-negative>self-positive neural activation and greater depressive symptoms at T1 and T2 in adolescents ($p_{-uncorr}$<.001 voxelwise threshold; p_{-fwe}<.05 clusterwise threshold).

T1 Depressive Symptoms				Peak Voxel Coordinates				
	Hem.	*Region*	*Brodmann Area*	*x*	*Y*	*Z*	*k*	*t-statistic (df=37)*
Self-Negative > Self-Positive								
	R/L	Caudate/putamen	48	10	10	2	1269	5.75
	R	Visual association	18	18	-84	-12	989	5.26
	L/R	dACC/SMA	6/24/32	-8	-4	52	351	4.76
	L	Somatosensory cortex /PPC	1/40	-36	-26	50	477	4.37
Self-Positive > Self-Negative (n/s)								
T2 Depressive Symptoms (controlling for T1 Depressive Sx)				Peak Voxel Coordinates				
	Hem.	*Region*	*Brodmann Area*	*x*	*Y*	*Z*	*k*	*t-statistic (df=35)*
Self-Negative > Self-Positive								
	L	insula	13	-48	-12	6	161	4.24
Self-Positive > Self-Negative (n/s)								

Note: R=right, L=left; dACC/SMA=dorsal anterior cingulate cortex/supplementary motor area; PPC=posterior parietal cortex; Sx=symptoms.

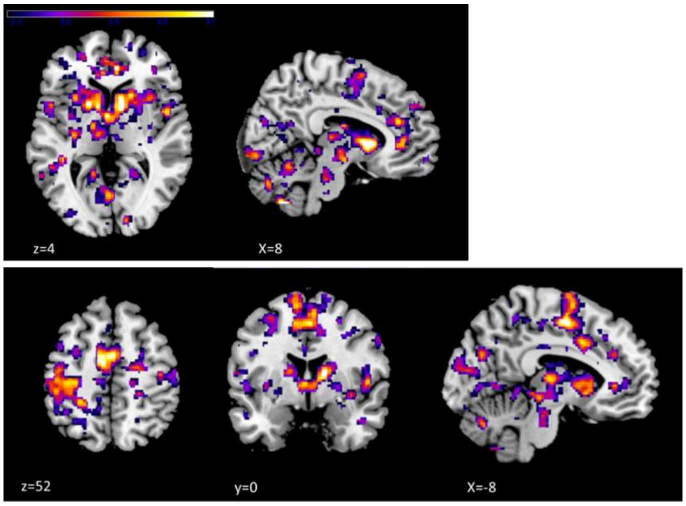

Figure 6. Significant activation during Self-Negative, relative to Self-Positive, condition associated with higher T1 depressive symptoms ($p_{\text{-}uncorr}$<.001 voxelwise threshold; $p_{\text{-}fwe}$<.05 clusterwise threshold).

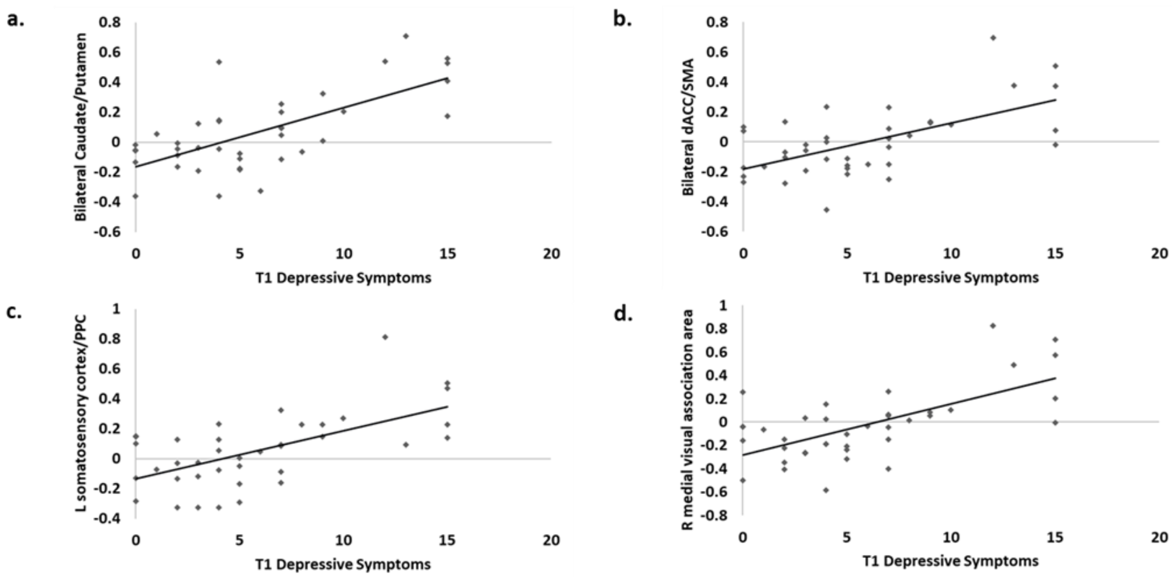

Figure 7. Relationships between adolescents' reports of depressive symptoms at T1 and neural response from Self-Negative>Self-Positive contrast in the: a) bilateral caudate/putamen; b) bilateral dorsal anterior cingulate/supplementary motor area; c) left somatosensory cortex/posterior parietal cortex; and d) right medial visual association area. Note: Average brain activation parameter estimates extracted from regression results using $p_{-uncorr}$<.001 voxelwise, p_{-fwe}<.05 clusterwise thresholds; L=left, R=right; positive numbers reflect more activation during self-negative condition, negative numbers reflect more activation during self-positive condition.

4.2.2.2 T2 Depressive Symptoms

Analyses controlled for T1 depressive symptoms. Higher levels of depressive symptoms at T2 were associated with greater brain activation during the Self-Negative, relative to Self-Positive, condition in the left insula ($p_{-uncorr}$<.001 voxelwise, p_{-FWE}<.05 cluster threshold) (Table 6, Figure 8); however, no significant results were found using the self-referential processing mask. Parameter estimates of activation for this cluster were extracted and used in individual regression analyses to measure potential effects of covariates on T2 depressive symptoms. In addition to brain activation, a main effect of T1 depressive symptoms was found when predicting T2 depressive symptoms (B=.911, SE=.191, p<.001). No main or interaction effects were found with age (ps>.60), pubertal status (ps>.59), or SES (ps>.24). No correlations were found between brain activation to Self-Positive>Self-Negative and T2 depressive symptoms.

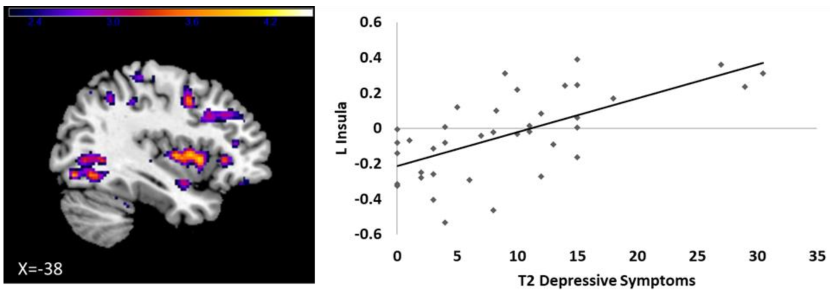

Figure 8. Relationship between adolescents' reports of depressive symptoms at T2 and neural response from Self-Negative>Self-Positive contrast in the left insula. Note: Average brain activation parameter estimates extracted from regression results using $p_{\text{-}uncorr}$<.001 voxelwise, $p_{\text{-}fwe}$<.05 clusterwise thresholds; L=left; positive numbers reflect more activation during self-negative condition, negative numbers reflect more activation during self-positive condition.

4.2.3 Aim 3

To test indirect effect models of neural self-referential processing and adolescent depressive symptoms. Using average activation within clusters found to be significantly activated during the Self-Negative>Self-Positive (n=4) and Self-Negative<Self-Positive (n=1) contrasts (see Table 3; IVs), separate models were used to analyze whether neural activation in each cluster predicted depressive symptoms (DV) through the indirect effects of three independent mediators,

including self-reported global self-worth, social self-competence and in-vivo self-perception ratings of self-concept (MEDs). It is important to note that this aim involved many tests (n=30, 15 per timepoint). Given that this is the first study to examine these associations, there was no correction for multiple comparisons. However, results should be viewed as preliminary.

4.2.3.1 T1 Depressive Symptoms

Bivariate correlations showed that all three measures of self-concept used as independent mediators were significantly associated with T1 depressive symptoms. Higher levels of global worth (r=-.345, p=.031), social self-competence (r=-.332, p=.039), and in-vivo self-perceptions (r=-.495, p=.001) were associated with lower levels of T1 depressive symptoms. Total effects computed in the Process models indicated that neural activation (i.e., the IVs) in the left VLPFC (B=6.82, SE=3.20, p=.04), left MPFC (B=8.50, SE=3.65, p=.03), and left SMA/dMPFC, (B=9.88, SE=4.92, p=.05) were significantly associated with T1 depressive symptoms (i.e., the DV); neural activation in the bilateral visual association clusters were not associated with depressive symptoms (ps>.09). Total effects of the left VLPFC and the left MPFC predicting depressive symptoms were maintained when accounting for covariates in the models. Tables 7, 8, and 9 present full model information using global worth, social self-competence, and in-vivo self-perceptions as mediators, respectively.

No significant indirect effects of global self-worth were found across all five models using global self-worth as a mediator, as the neural activation within each of the five clusters used as IVs were not significantly associated with adolescents' reports of global self-worth (ps>.16). Likewise, no significant indirect effects of social self-competence were found across all five models using social self-competence as a mediator, as neural activation within each of the five clusters (IVs) were not significantly associated with adolescents' reports of social self-competence (*ps*>.06).

Using in-vivo self-perceptions as the mediator, two of the five models yielded significant indirect effects. Neural activation in the left dMPFC was associated with T1 depressive symptoms through the indirect effect of in-vivo self-perceptions (Effect=3.162, BootSE=2.027; 95%CI: 0.077, 7.801). Greater dMPFC activation during the Self-Negative condition, relative to Self-Positive, was related to higher T1 depressive symptoms, through lower (i.e., more negative) in-vivo self-perception ratings (Figure 9a). Neural activation in the right visual association area was also associated with T1 depressive symptoms through the indirect effects of in-vivo self-perceptions (Effect=-3.922, BootSE=2.237; 95%CI: -273, -8.971). Greater neural activation in the visual association area during the *Self-Positive* condition, relative to Self-Negative, was associated with lower levels of T1 depressive symptoms, through more positive in-vivo self-perception ratings (Figure 9b). When controlling for covariates in the model, both indirect effect findings became non-significant. In these models, SES was significantly associated with behavioral reports of self-perceptions (MPFC: B=2.9774, SE=1.2610, p=.02; visual association area: B=3.2388, SE=1.3038, p=.02). There were no other significant effects due to covariates in the models.

Table 7. Direct and indirect effects of neural activation on T1 Depressive Symptoms through adolescents' global self-worth.

	NO COVARIATES				*WITH COVARIATES (Age, Puberty, SES)*			
Independent Variable	*Coeff.*	*SE*	*t-statistic*	*p*	*Coeff.*	*SE*	*t-statistic*	*p*
Self Negative > Self Positive								
L VLPFC (BA45)								
Total Effect Model Summary	**R^2=.109, *F(1, 37)* = 4.535, *p*=.040**				R^2=.211, *F(4, 34)*=2.273, *p*=.082			
Effect of IV on mediator	-.357	.345	-1.036	.301	-.301	.347	-.869	.391
Direct effect of mediator on DV	-2.894	1.472	-1.967	.057	-2.649	1.556	-1.703	.098
Direct effect of IV on DV	5.790	3.131	1.849	.073	5.954	3.1872	1.872	.070
Total effect of IV on DV	**6.824**	3.204	2.130	.040	**6.752**	3.233	2.089	.044
Indirect effect of IV on DV	Effect=1.033 (BootSE=.333), 95%CI: -0.158, 5.423				Effect=.798 (BootSE=1.544), 95%CI: -0.832, 5.124			
Standardized indirect effect	Effect=.050 (BootSE=.068), 95%CI: -0.036, .226				Effect=.039 (BootSE=.068), 95%CI: -0.044, .216			
L dMPFC (BA8)								
Total Effect Model Summary	**R^2=.128, *F(1, 37)* = 5.414, *p*=.026**				R^2=.218, *F(4, 34)*=2.367, *p*=.072			
Effect of IV on mediator	-.330	.399	-.827	.413	-.302	.399	-.758	.454
Direct effect of mediator on DV	**-2.937**	1.444	-2.033	.040	-2.683	1.542	-1.740	.091
Direct effect of IV on DV	**7.529**	3.540	2.127	.040	7.187	3.616	1.988	.055
Total effect of IV on DV	**8.499**	3.653	2.327	.026	**7.998**	3.691	2.167	.037
Indirect effect of IV on DV	Effect=.970 (BootSE=1.726), 95%CI: -1.389, 5.613				Effect=.811 (BootSE=1.772), 95%CI: -1.485, 5.719			
Standardized indirect effect	Effect=.041 (BootSE=.068), 95%CI: -0.063, .208				Effect=.034 (BootSE=.070), 95%CI: -0.063, .218			
L SMA/dMPFC (BA6/8)								
Total Effect Model Summary	**R^2=.099, *F(1, 37)* = 4.042, *p*=.052**				R^2=.182, *F(4, 34)*=1.894, *p*=.134			
Effect of IV on mediator	-.744	.519	-1.433	.160	-.589	.520	-1.132	.266
Direct effect of mediator on DV	-2.800	1.508	-1.857	.072	-2.641	1.599	-1.651	.108
Direct effect of IV on DV	7.801	4.892	1.595	.120	7.076	4.941	1.432	.162
Total effect of IV on DV	**9.884**	4.916	2.010	.052	8.631	4.972	1.736	.092
Indirect effect of IV on DV	Effect=2.083 (BootSE=2.569), 95%CI: -0.755, 9.315				Effect=1.555 (BootSE=2.673), 95%CI: -1.317, 9.030			
Standardized indirect effect	Effect=.066 (BootSE=.072), 95%CI: -0.025, .252				Effect=.050 (BootSE=.076), 95%CI: -0.042, .261			
L Visual association (BA18)								
Total Effect Model Summary	R^2=.076, *F(1, 37)* = 3.033, *p*=.090				R^2=.169, *F(4, 34)*=1.730, *p*=.166			
Effect of IV on mediator	-.020	.385	-.052	.959	-.145	.401	-.363	.719
Direct effect of mediator on DV	**-3.329**	1.453	-2.291	.028	-2.932	1.569	-1.869	.071
Direct effect of IV on DV	6.188	3.402	1.819	.077	5.491	3.671	1.496	.144
Total effect of IV on DV	6.255	3.591	1.742	.090	5.917	3.796	1.559	.128
Indirect effect of IV on DV	Effect=.066 (BootSE=1.342), 95%CI: -2.344, 3.158				Effect=.426 (BootSE=1.490), 95%CI: -2.266, 3.966			
Standardized indirect effect	Effect=.003 (BootSE=.056), 95%CI: -0.099, .128				Effect=.019 (BootSE=.062), 95%CI: -0.093, .164			
Self Positive > Self Negative								
R Visual association (BA18)								
Total Effect Model Summary	R^2=.024, *F(1, 37)* = 0.896, p=.350				R^2=.124, *F(4, 34)*=1.199, p=.329			
Effect of IV on mediator	.111	.391	.285	.778	.082	.385	.214	.832
Direct effect of mediator on DV	**-3.289**	1.504	-2.187	.035	-3.037	1.608	-1.889	.068
Direct effect of IV on DV	-3.189	3.582	-.890	.379	-2.488	3.607	-.690	.495
Total effect of IV on DV	-3.555	3.756	-.946	.350	-2.738	3.739	-.732	.469
Indirect effect of IV on DV	Effect=-.366 (BootSE=1.617), 95%CI: -4.551, 2.091				Effect=-.250 (BootSE=1.852), 95%CI: -5.546, 2.040			
Standardized indirect effect	Effect=-.016 (BootSE=.065), 95%CI: -0.172, .092				Effect=-.011 (BootSE=.074), 95%CI: -.217, .089			

Bolded parameter=$p \leq .05$; Note: IV=independent variable; DV=dependent variable; L=left; R=right, VLPFC=ventrolateral prefrontal cortex; DLPFC=dorsolateral prefrontal cortex; SMA/dMPFC= supplementary motor area/dorsal medial prefrontal cortex. All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Negative>Self-Positive contrast.

Table 8. Direct and indirect effects of neural activation on T1 Depressive Symptoms through adolescents' feelings of Social Self-Competence.

	NO COVARIATES				*WITH COVARIATES (Age, Puberty, SES)*			
Independent Variable	*Coeff.*	*SE*	*t-statistic*	*p*	*Coeff.*	*SE*	*t-statistic*	*p*
L VLPFC (BA45)								
Total Effect Model Summary	**R^2=.109, $F(1, 37)$ = 4.535, p=.040**				R^2=.211, $F(4, 34)$=2.273, p=.082			
Effect of IV on mediator	.621	.512	1.213	.233	.777	.496	1.567	.126
Direct effect of mediator on DV	**-2.678**	.943	-2.841	.008	**-2.823**	1.023	-2.759	.009
Direct effect of IV on DV	**8.487**	2.994	2.835	.008	**8.945**	3.063	2.921	.006
Total effect of IV on DV	**6.824**	3.204	2.130	.040	**6.752**	3.233	2.089	.044
Indirect effect of IV on DV	Effect=-1.663 (BootSE=1.193), 95%CI: -3.908, 0.924				Effect=-2.193 (BootSE=1.451), 95%CI: -5.030, .880			
Standardized indirect effect	Effect=-.081 (BootSE=.057), 95%CI: -0.189, .037				Effect=-.106 (BootSE=.068), 95%CI: -0.239, .038			
L dMPFC (BA8)								
Total Effect Model Summary	**R^2=.128, $F(1, 37)$ = 5.414, p=.026**				R^2=.218, $F(4, 34)$=2.367, p=.072			
Effect of IV on mediator	.788	.587	1.342	.188	.879	.569	1.545	.132
Direct effect of mediator on DV	**-2.785**	.927	-3.006	.005	**-2.830**	1.016	-2.785	.009
Direct effect of IV on DV	**10.695**	3.391	3.154	.003	**10.487**	3.488	3.007	.005
Total effect of IV on DV	**8.499**	3.653	2.327	.026	**7.998**	3.691	2.167	.037
Indirect effect of IV on DV	Effect=-2.196 (BootSE=1.752), 95%CI: -6.175, .648				Effect=-2.488 (BootSE=2.127), 95%CI: -7.309, 1.068			
Standardized indirect effect	Effect=-.092 (BootSE=.076), 95%CI: -0.270, .024				Effect=-.105 (BootSE=.092), 95%CI: -0.320, .040			
L SMA/dMPFC (BA6/8)								
Total Effect Model Summary	**R^2=.099, $F(1, 37)$ = 4.042, p=.052**				R^2=.182, $F(4, 34)$=1.894, p=.134			
Effect of IV on mediator	.931	.782	1.192	.241	1.255	.745	1.685	.101
Direct effect of mediator on DV	**-2.645**	.951	-2.781	.009	**-2.793**	1.055	-2.646	.012
Direct effect of IV on DV	**12.347**	4.608	2.680	.011	**12.136**	4.771	2.544	.016
Total effect of IV on DV	**9.884**	4.916	2.010	.052	8.631	4.972	1.736	.092
Indirect effect of IV on DV	Effect=-2.463 (BootSE=1.892), 95%CI: -6.992, .307				Effect=-3.505 (BootSE=2.671), 95%CI: -10.030, .072			
Standardized indirect effect	Effect=-.078 (BootSE=.054), 95%CI: -0.198, .010				Effect=-.111 (BootSE=.076), 95%CI: -0.287, .003			
L Visual association (BA18)								
Total Effect Model Summary	R^2=.076, $F(1, 37)$ = 3.033, p=.090				R^2=.169, $F(4, 34)$=1.730, p=.166			
Effect of IV on mediator	.671	.564	1.190	.242	.518	.581	.892	.379
Direct effect of mediator on DV	**-2.595**	.969	-2.677	.024	**-2.363**	1.061	-2.226	.033
Direct effect of IV on DV	**7.996**	3.388	2.360	.024	7.141	3.635	1.965	.058
Total effect of IV on DV	6.255	3.591	1.742	.090	5.917	3.796	1.559	.128
Indirect effect of IV on DV	Effect=-1.742 (BootSE=2.420), 95%CI: -8.279, .965				Effect=-1.224 (BootSE=2.229), 95%CI: -7.236, 1.818			
Standardized indirect effect	Effect=-.077 (BootSE=.096), 95%CI: -0.323, .045				Effect=-.054 (BootSE=.089), 95%CI: -0.280, .084			
Self Positive > Self Negative								
R Visual association (BA18)								
Total Effect Model Summary	R^2=.024, $F(1, 37)$ = 0.896, p=.350				R^2=.124, $F(4, 34)$=1.199, p=.329			
Effect of IV on mediator	-1.097	.556	-1.972	.056	**-1.150**	.528	-2.180	.036
Direct effect of mediator on DV	**-2.722**	1.030	-2.643	.012	**-2.666**	1.143	-2.333	.026
Direct effect of IV on DV	-6.540	3.664	-1.785	.083	-5.804	3.754	-1.546	.132
Total effect of IV on DV	-3.555	3.756	-.946	.350	-2.738	3.739	-.732	.469
Indirect effect of IV on DV	Effect=2.985 (BootSE=1.889), 95%CI: -.159, 7.099				Effect=3.066 (BootSE=2.081), 95%CI: -.400, 7.666			
Standardized indirect effect	Effect=.129 (BootSE=.077), 95%CI: -0.007, .286				Effect=.133 (BootSE=.085), 95%CI: -0.017, .310			

Bolded parameter=$p \leq .05$; Note: IV=independent variable; DV=dependent variable; L=left; R=right, VLPFC=ventrolateral prefrontal cortex; DLPFC=dorsolateral prefrontal cortex; SMA/dMPFC= supplementary motor area/dorsal medial prefrontal cortex. All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Negative>Self-Positive contrast.

Table 9. Direct and indirect effects of neural activation on T1 Depressive Symptoms through adolescents' feelings of In-Vivo Self-Perception Ratings.

	NO COVARIATES				*WITH COVARIATES (Age, Puberty, SES)*			
Independent Variable	*Coeff.*	*SE*	*t-statistic*	*p*	*Coeff.*	*SE*	*t-statistic*	*p*
Self Negative > Self Positive								
L VLPFC (BA45)								
Total Effect Model Summary	**R^2=.109, *F(1, 37)* = 4.535, p=.040**				R^2=.211, *F(4, 34)*=2.273, p=.082			
Effect of IV on mediator	-14.515	9.186	-1.580	.123	-11.421	9.052	-1.262	.216
Direct effect of mediator on DV	**-.157**	.052	-3.031	.005	**-.142**	.057	-2.489	.018
Direct effect of IV on DV	4.541	2.996	1.516	.138	5.131	3.081	1.666	.105
Total effect of IV on DV	**6.824**	3.204	2.130	.040	**6.752**	3.233	2.089	.044
Indirect effect of IV on DV	Effect=2.283 (BootSE=1.871), 95%CI: -0.439, 6.631				Effect=1.622 (BootSE=1.733), 95%CI: -0.9242, 5.869			
Standardized indirect effect	Effect=.111 (BootSE=.082), 95%CI: -0.023, .296				Effect=.079 (BootSE=.078), 95%CI: -0.044, .257			
L dMPFC (BA8)								
Total Effect Model Summary	**R^2=.128, *F(1, 37)* = 5.414, p=.026**				R^2=.218, *F(4, 34)*=2.367, p=.072			
Effect of IV on mediator	**-20.806**	10.385	-2.004	.053	-17.341	10.195	-1.701	.098
Direct effect of mediator on DV	**-.152**	.053	-2.874	.007	**-.137**	.058	-2.341	.025
Direct effect of IV on DV	5.338	3.516	1.518	.138	5.629	3.614	1.558	.129
Total effect of IV on DV	**8.499**	3.653	2.327	.026	**7.998**	3.691	2.167	.037
Indirect effect of IV on DV	**Effect=3.162 (BootSE=2.027), 95%CI: 0.077, 7.801**				Effect=2.369 (BootSE=1.910), 95%CI: -0.519, 6.814			
Standardized indirect effect	**Effect=.133 (BootSE=.078), 95%CI: 0.004, .305**				Effect=.100 (BootSE=.077), 95%CI: -0.022, .272			
L SMA/dMPFC(BA6/8)								
Total Effect Model Summary	R^2=.099, *F(1, 37)* = 4.042, p=.052				R^2=.182, *F(4, 34)*=1.894, p=.134			
Effect of IV on mediator	-17.621	14.183	-1.242	.222	-11.276	13.857	-.814	.422
Direct effect of mediator on DV	**-.161**	.051	-3.148	.003	**-.150**	.057	-2.651	.012
Direct effect of IV on DV	7.046	4.505	1.564	.127	6.936	4.627	1.499	.143
Total effect of IV on DV	**9.884**	4.916	2.010	.052	8.631	4.972	1.736	.092
Indirect effect of IV on DV	Effect=2.838 (BootSE=2.903), 95%CI: -1.475, 9.947				Effect=1.695 (BootSE=2.660), 95%CI: -2.190, 8.332			
Standardized indirect effect	Effect=.090 (BootSE=.081), 95%CI: -0.051, .270				Effect=.054 (BootSE=.075), 95%CI: -0.077, .230			
L Visual association (BA18)								
Total Effect Model Summary	R^2=.076, *F(1, 37)* = 3.033, p=.090				R^2=.169, *F(4, 34)*=1.730, p=.166			
Effect of IV on mediator	-3.505	10.428	-.336	.739	-.758	10.597	-.072	.943
Direct effect of mediator on DV	**-.172**	.050	-3.463	.001	**-.161**	.06	-2.889	.007
Direct effect of IV on DV	5.651	3.158	1.789	.082	5.795	3.443	1.683	.102
Total effect of IV on DV	6.255	3.591	1.742	.090	5.917	3.796	1.559	.128
Indirect effect of IV on DV	Effect=.603 (BootSE=1.767), 95%CI: -2.335, 4.688				Effect=.122 (BootSE=1.900), 95%CI: -3.849, 3.935			
Standardized indirect effect	Effect=.027 (BootSE=.073), 95%CI: -0.110, .183				Effect=.005 (BootSE=.081), 95%CI: -0.172, .159			
Self Positive > Self Negative								
R Visual association (BA18)								
Total Effect Model Summary	R^2=.024, *F(1, 37)* = 0.896, p=.350				R^2=.124, *F(4, 34)*=1.199, p=.329			
Effect of IV on mediator	**21.914**	9.999	2.192	.035	**20.016**	9.565	2.093	.044
Direct effect of mediator on DV	**-.179**	.055	-3.251	.003	**-.165**	.062	-2.682	.011
Direct effect of IV on DV	.368	3.559	.103	.918	.572	3.653	.157	.877
Total effect of IV on DV	-3.555	3.756	-.946	.350	-2.738	3.739	-.732	.469
Indirect effect of IV on DV	**Effect=-3.922 (BootSE=2.195 95%CI: -8.825, -.329**				Effect=-3.310 (BootSE=2.201), 95%CI: -8.314, 0.131			
Standardized indirect effect	**Effect=-.170 (BootSE=.086), 95%CI: -0.350, -.015**				Effect=-.143 (BootSE=.089), 95%CI: -0.338, .006			

Bolded parameter=$p \leq .05$; Note: IV=independent variable; DV=dependent variable; L=left; R=right, VLPFC=ventrolateral prefrontal cortex; DLPFC=dorsolateral prefrontal cortex; SMA/dMPFC= supplementary motor area/dorsal medial prefrontal cortex. All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Negative>Self-Positive contrast.

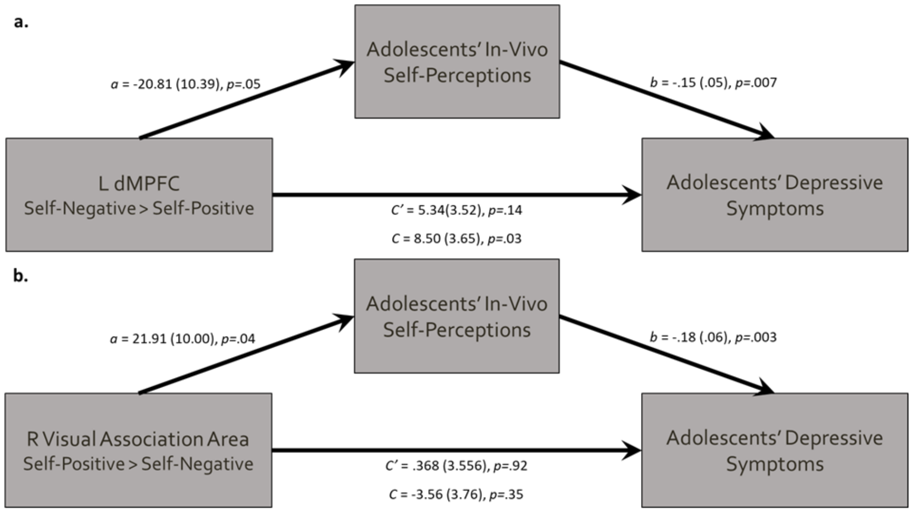

Figure 9. Neural activation during self-referential processing is associated with concurrent depressive symptoms due to significant indirect effects of a) Self-Negative>Self-Positive activation in the left dorsal medial prefrontal cortex (L dMPFC) and b) Self-Positive>Self-Negative activation in the right visual association area; Note: L=left, R=right; MPFC=medial prefrontal cortex.

4.2.3.2 T2 Depressive Symptoms

Bivariate correlations showed that two of the three measures of self-concept used as independent mediators were significantly associated with T2 depressive symptoms. Higher levels of global worth (r=-.478, p=.002) and more positive in-vivo self-perceptions (r=-.495, p=.002) were associated with lower levels of T2 depressive symptoms. Social self-competence was not significantly correlated with T2 symptoms (r=-.151, p=.364). All indirect models controlled for T1 depressive symptoms. Total effects computed in the Process models indicated that neural activation (i.e., the IVs) was not significantly associated with T2 depressive symptoms (i.e., the DV), for all five clusters (*ps*>.07). Tables 10, 11, and 12 present full model information using global worth, social self-competence, and in-vivo self-perceptions as mediators, respectively.

No significant indirect effects were found using global self-worth, social self-competence, or in-vivo self-perceptions as mediators. When controlling for covariates in the model, all findings remained non-significant.

Table 10. Direct and indirect effects of neural activation on T2 Depressive Symptoms through adolescents' feelings of Global Self-Worth.

	CONTROLLING FOR T1 MFQ				*WITH COVARIATES (Age, Puberty, SES)*			
Independent Variable	*Coeff.*	*SE*	*t-statistic*	*p*	*Coeff.*	*SE*	*t-statistic*	*p*
Self Negative > Self Positive								
L VLPFC (BA45)								
Total Effect Model Summary	**R^2=.491, *F(2, 35)* = 16.904, p<.001**				**R^2=.510, *F(5, 32)*=6.647, p<.001**			
Effect of IV on mediator	-.129	.357	-0.361	.720	-.099	.364	-.273	.787
Direct effect of mediator on DV	**-4.721**	2.031	-2.324	.026	-4.422	2.242	-1.973	.058
Direct effect of IV on DV	7.037	4.296	1.638	.111	7.240	4.618	1.568	.127
Total effect of IV on DV	7.645	4.550	1.680	.102	7.679	4.817	1.594	.127
Indirect effect of IV on DV	Effect=.608 (BootSE=1.994), 95%CI: -2.502, 5.796				Effect=.438 (BootSE=2.124), 95%CI: -2.788, 6.094			
Standardized indirect effect	Effect=.017 (BootSE=.050), 95%CI: -0.069, .134				Effect=.012 (BootSE=.052), 95%CI: -0.078, .142			
L dMPFC (BA8)								
Total Effect Model Summary	**R^2=.453, *F(2, 35)* = 14.476, p<.001**				**R^2=.473, *F(5, 32)*=5.744, p=.001**			
Effect of IV on mediator	-.029	.418	-.068	.946	-.042	.420	-.100	.921
Direct effect of mediator on DV	**-4.914**	2.101	-2.339	.025	-4.577	2.322	-1.971	.058
Direct effect of IV on DV	2.029	5.200	.390	.699	2.034	5.522	.368	.715
Total effect of IV on DV	2.169	5.522	.393	.697	2.226	5.765	.386	.702
Indirect effect of IV on DV	Effect=.140 (BootSE=2.434), 95%CI: -4.176, 6.078				Effect=.192 (BootSE=2.540), 95%CI: -3.763, 6.722			
Standardized indirect effect	Effect=.003 (BootSE=.055), 95%CI: -0.092, .134				Effect=.005 (BootSE=.056), 95%CI: -0.082, .140			
L SMA/dMPFC (BA6/8)								
Total Effect Model Summary	**R^2=.501, *F(2, 35)* = 17.602, p<.001**				**R^2=.517, *F(5, 32)*=6.841, p<.001**			
Effect of IV on mediator	-.446	.540	-.826	.415	-.361	.539	-.669	.508
Direct effect of mediator on DV	**-4.451**	2.044	-2.178	.037	-4.173	2.253	-1.852	.074
Direct effect of IV on DV	11.029	6.591	1.673	.103	10.956	6.924	1.582	.124
Total effect of IV on DV	13.013	6.868	1.895	.066	12.462	7.132	1.747	.090
Indirect effect of IV on DV	Effect=1.984 (BootSE=3.143), 95%CI: -2.810, 9.964				Effect=1.506 (BootSE=3.094), 95%CI: -3.772, 9.106			
Standardized indirect effect	Effect=.037 (BootSE=.053), 95%CI: -0.052, .162				Effect=.028 (BootSE=.052), 95%CI: -0.070, .147			
L Visual association (BA18)								
Total Effect Model Summary	**R^2=.457, *F(2, 35)* = 14.710, p<.001**				**R^2=.484, *F(5, 32)*=6.005, p=.001**			
Effect of IV on mediator	.246	.399	.618	.541	.082	.418	.197	.845
Direct effect of mediator on DV	**-5.127**	2.091	-2.453	.020	**-4.674**	2.289	-2.042	.050
Direct effect of IV on DV	4.644	4.958	.937	.356	5.584	5.409	1.032	.310
Total effect of IV on DV	3.381	5.273	.641	.526	5.200	5.668	.918	.366
Indirect effect of IV on DV	Effect=-1.263 (BootSE=2.233), 95%CI: -5.703, 3.825				Effect=-.384 (BootSE=2.230), 95%CI: -4.686, 4.676			
Standardized indirect effect	Effect=-.030 (BootSE=.051), 95%CI: -0.134, .078				Effect=-.009 (BootSE=.050), 95%CI: -0.105, .105			
Self Negative < Self Positive								
R Visual association (BA18)								
Total Effect Model Summary	**R^2=.476, *F(2, 35)* = 15.881, p<.001**				**R^2=.499, *F(5, 32)*=6.372, p<.001**			
Effect of IV on mediator	-.004	.407	-.009	.993	.040	.404	.098	.923
Direct effect of mediator on DV	**-4.928**	2.048	-2.406	.022	**-4.538**	2.259	-2.009	.053
Direct effect of IV on DV	-6.870	4.931	-1.393	.173	-7.093	5.163	-1.374	.179
Total effect of IV on DV	-6.852	5.258	-1.303	.201	-7.273	5.402	-1.346	.188
Indirect effect of IV on DV	Effect=.019 (BootSE=2.665), 95%CI: -6.881, 3.853				Effect=-.179 (BootSE=2.846), 95%CI: -7.899, 3.990			
Standardized indirect effect	Effect=.001 (BootSE=.058), 95%CI: -0.134, .097				Effect=-.004 (BootSE=.062), 95%CI: -0.153, .099			

Bolded parameter=$p<.05$; Note: IV=independent variable; DV=dependent variable; L=left; R=right, VLPFC=ventrolateral prefrontal cortex; DLPFC=dorsolateral prefrontal cortex; SMA/dMPFC= supplementary motor area/dorsal medial prefrontal cortex. All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Negative>Self-Positive contrast.

Table 11. Direct and indirect effects of neural activation on T2 Depressive Symptoms through adolescents' feelings of Social Self-Competence.

	CONTROLLING FOR T1 MFQ				*WITH COVARIATES (Age, Puberty, SES)*			
Independent Variable	*Coeff.*	*SE*	*t-statistic*	*p*	*Coeff.*	*SE*	*t-statistic*	*p*
L VLPFC (BA45)								
Total Effect Model Summary	**R^2=.491, $F(2, 35)$ = 16.904, p<.001**				**R^2=.510, $F(5, 32)$=6.647, p<.001**			
Effect of IV on mediator	**1.083**	.500	2.167	.037	**1.209**	.481	2.515	.017
Direct effect of mediator on DV	-.438	1.559	-.281	.781	.344	1.799	.191	.850
Direct effect of IV on DV	8.119	4.911	1.653	.108	7.263	5.352	1.357	.185
Total effect of IV on DV	7.645	4.550	1.680	.102	7.679	4.817	1.594	.121
Indirect effect of IV on DV	Effect=-.474 (BootSE=1.797), 95%CI: -4.494, 2.702				Effect=.416 (BootSE=1.863), 95%CI: -3.269, 4.209			
Standardized indirect effect	Effect=-.013 (BootSE=.049), 95%CI: -0.120, .080				Effect=.012 (BootSE=.052), 95%CI: -0.084, .129			
L dMPFC (BA8)								
Total Effect Model Summary	**R^2=.453, $F(2, 35)$ = 14.476, p<.001**				**R^2=.473, $F(5, 32)$=5.744, p=.001**			
Effect of IV on mediator	**1.463**	.572	2.558	.015	**1.478**	.548	2.695	.011
Direct effect of mediator on DV	.256	1.656	.154	.878	1.297	1.874	.692	.494
Direct effect of IV on DV	1.795	6.102	.294	.770	.309	6.438	.048	.962
Total effect of IV on DV	2.169	5.522	.393	.697	2.226	5.765	.386	.702
Indirect effect of IV on DV	Effect=.374 (BootSE=2.654), 95%CI: -6.047, 4.910				Effect=1.917 (BootSE=2.879), 95%CI: -3.862, 8.170			
Standardized indirect effect	Effect=.009 (BootSE=.064), 95%CI: -0.141, .128				Effect=.046 (BootSE=.071), 95%CI: -0.088, .207			
L SMA/dMPFC (BA6/8)								
Total Effect Model Summary	**R^2=.501, $F(2, 35)$ = 17.602, p<.001**				**R^2=.501, $F(5, 32)$ = 17.602, p<.001**			
Effect of IV on mediator	**1.544**	.769	2.010	.052	**1.727**	.723	2.390	.023
Direct effect of mediator on DV	-.472	1.531	-.308	.760	.287	1.771	.162	.873
Direct effect of IV on DV	13.741	7.349	1.870	.070	11.967	7.863	1.522	.138
Total effect of IV on DV	13.013	6.868	1.895	.066	12.462	7.132	1.747	.090
Indirect effect of IV on DV	Effect=-.728 (BootSE=2.659), 95%CI: -6.896, 3.900				Effect=.495 (BootSE=2.911), 95%CI: -6.328, 5.621			
Standardized indirect effect	Effect=-.013 (BootSE=.047), 95%CI: -0.116, .077				Effect=.009 (BootSE=.053), 95%CI: -0.114, .108			
L Visual association (BA18)								
Total Effect Model Summary	**R^2=.457, $F(2, 35)$ = 14.710, p<.001**				**R^2=.484, $F(5, 32)$=6.005, p=.001**			
Effect of IV on mediator	**1.281**	.556	2.302	.027	1.053	.574	1.834	.076
Direct effect of mediator on DV	.117	1.626	.072	.943	.957	1.765	.542	.592
Direct effect of IV on DV	3.231	5.740	.563	.577	4.192	6.025	.696	.492
Total effect of IV on DV	3.381	5.273	.641	.526	5.200	5.668	.918	.366
Indirect effect of IV on DV	Effect=.150 (BootSE=3.266), 95%CI: -9.339, 4.659				Effect=1.008 (BootSE=2.616), 95%CI: -6.289, 5.046			
Standardized indirect effect	Effect=.004 (BootSE=.077), 95%CI: -0.197, .126				Effect=.024 (BootSE=.063), 95%CI: -0.131, .142			
Self Positive > Self Negative								
R Visual association (BA18)								
Total Effect Model Summary	**R^2=.476, $F(2, 35)$ = 15.881, p<.001**				**R^2=.499, $F(5, 32)$= 6.372, p<.001**			
Effect of IV on mediator	**-1.315**	.564	-2.333	.026	**-1.242**	.541	-2.297	.028
Direct effect of mediator on DV	-.291	1.599	-.182	.857	.591	1.791	.330	.744
Direct effect of IV on DV	-7.235	5.731	-1.262	.215	-6.539	5.913	-1.106	.277
Total effect of IV on DV	-6.852	5.258	-1.303	.201	-7.273	5.402	-1.346	.188
Indirect effect of IV on DV	Effect=.383 (BootSE=2.323), 95%CI: -4.366, 5.296				Effect=-.734 (BootSE=2.201), 95%CI: -5.250, 3.732			
Standardized indirect effect	Effect=.009 (BootSE=.058), 95%CI: -0.117, .119				Effect=-.018 (BootSE=.057), 95%CI: -0.150, .081			

Bolded parameter=p<.05; Note: IV=independent variable; DV=dependent variable; L=left; R=right, VLPFC=ventrolateral prefrontal cortex; DLPFC=dorsolateral prefrontal cortex; SMA/dMPFC= supplementary motor area/dorsal medial prefrontal cortex. All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Negative>Self-Positive contrast.

Table 12. Direct and indirect effects of neural activation on T2 Depressive Symptoms through adolescents' feelings of In-Vivo Self-Perception Ratings.

	CONTROLLING FOR T1 MFQ				*WITH COVARIATES (Age, Puberty, SES)*			
Independent Variable	*Coeff.*	*SE*	*t-statistic*	*p*	*Coeff.*	*SE*	*t-statistic*	*p*
Self Negative > Self Positive								
L VLPFC (BA45)								
Total Effect Model Summary	**R^2=.491, $F(2, 35)$ = 16.904, p<.001**				**R^2=.510, $F(5, 32)$=6.647, p<.001**			
Effect of IV on mediator	6.924	4.497	1.540	.133	-3.883	9.098	-.427	.672
Direct effect of mediator on DV	-.127	.085	-1.499	.143	-.123	.093	-1.327	.194
Direct effect of IV on DV	6.924	4.497	1.540	.133	7.202	4.774	1.509	.142
Total effect of IV on DV	7.645	4.550	1.680	.102	7.679	4.817	1.594	.121
Indirect effect of IV on DV	Effect=.721 (BootSE=1.491), 95%CI: -2.578, 3.727				Effect=.477 (BootSE=1.508), 95%CI: -2.719, 3.615			
Standardized indirect effect	Effect=.020 (BootSE=.040), 95%CI: -0.070, .101				Effect=.0133 (BootSE=.040), 95%CI: -0.077, .093			
L dMPFC (BA8)								
Total Effect Model Summary	**R^2=.453, $F(2, 35)$ = 14.476, p<.001**				**R^2=.473, $F(5, 32)$=5.744, p=.001**			
Effect of IV on mediator	-10.601	10.355	-1.024	.313	-9.134	10.411	-.877	.387
Direct effect of mediator on DV	**-.139**	.088	-1.572	.125	-.131	.097	-1.352	.186
Direct effect of IV on DV	.697	5.490	.127	.900	1.033	5.760	.179	.859
Total effect of IV on DV	2.169	5.522	.393	.697	2.226	5.765	.386	.702
Indirect effect of IV on DV	Effect=1.472 (BootSE=1.928), 95%CI: -1.804, 5.964				Effect=1.193 (BootSE=1.966), 95%CI: -2.232, 5.938			
Standardized indirect effect	Effect=.035 (BootSE=.044), 95%CI: -0.044, .136				Effect=.028 (BootSE=.044), 95%CI: -0.050, .132			
L SMA/dMPFC (BA6/8)								
Total Effect Model Summary	**R^2=.501, $F(2, 35)$ = 17.602, p<.001**				**R^2=.517, $F(5, 32)$=6.841, p<.001**			
Effect of IV on mediator	-4.249	13.676	-.311	.758	-1.083	13.608	-.080	.937
Direct effect of mediator on DV	-.133	.083	-1.598	.119	-.131	.091	-1.438	.161
Direct effect of IV on DV	12.449	6.730	1.850	.073	12.320	7.017	1.756	.089
Total effect of IV on DV	13.013	6.868	1.895	.066	12.462	7.132	1.747	.090
Indirect effect of IV on DV	Effect=.564 (BootSE=2.558), 95%CI: -5.677, 5.279				Effect=.142 (BootSE=2.611), 95%CI: -6.659, 4.120			
Standardized indirect effect	Effect=.010 (BootSE=.045), 95%CI: -0.102, .088				Effect=.003 (BootSE=.046), 95%CI: -0.124, .068			
L Visual association (BA18)								
Total Effect Model Summary	**R^2=.457, $F(2, 35)$ = 14.710, p<.001**				**R^2=.484, $F(5, 32)$=6.005, p=.001**			
Effect of IV on mediator	5.669	10.026	.565	.575	6.836	10.398	.657	.516
Direct effect of mediator on DV	-.148	.087	-1.704	.098	-.145	.094	-1.541	.134
Direct effect of IV on DV	4.217	5.159	.817	.419	6.193	5.587	1.109	.276
Total effect of IV on DV	3.381	5.273	.641	.526	5.200	5.668	.918	.366
Indirect effect of IV on DV	Effect=-.836 (BootSE=1.905), 95%CI: -5.828, 1.962				Effect=-.994 (BootSE=2.066), 95%CI: -6.576, 1.859			
Standardized indirect effect	Effect=-.020 (BootSE=.045), 95%CI: -0.140, .041				Effect=-.024 (BootSE=.048), 95%CI: -0.152, .042			
Self Positive> Self Negative								
R Visual association (BA18)								
Total Effect Model Summary	**R^2=.476, $F(2, 35)$ = 15.881, p<.001**				**R^2=.499, $F(5, 32)$=6.372, p<.001**			
Effect of IV on mediator	19.268	9.691	1.988	.055	19.061	9.547	1.997	.054
Direct effect of mediator on DV	-.117	.091	-1.282	.209	-.102	.100	-1.024	.314
Direct effect of IV on DV	-4.607	5.496	-.838	.408	-5.322	5.724	-.930	.360
Total effect of IV on DV	-6.852	5.258	-1.303	.201	-7.273	5.402	-1.346	.188
Indirect effect of IV on DV	Effect=-2.245 (BootSE=2.243), 95%CI: -7.614, 1.346				Effect=-1.951 (BootSE=2.099), 95%CI: -6.745, 1.603			
Standardized indirect effect	Effect=-.054 (BootSE=.051), 95%CI: -0.165, .036				Effect=-.047 (BootSE=.048), 95%CI: -0.150, .040			

Bolded parameter=$p<.05$; Note: IV=independent variable; DV=dependent variable; L=left; R=right, VLPFC=ventrolateral prefrontal cortex; DLPFC=dorsolateral prefrontal cortex; SMA/dMPFC= supplementary motor area/dorsal medial prefrontal cortex. All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Negative>Self-Positive contrast.

5.0 Discussion

The current study demonstrates that adolescents' neural activation during the processing of affectively valenced, self-referential information is directly associated with both adolescents' reports of self-concept, particularly within the social domain, and depressive symptoms. As expected, primary findings showed that adolescents who exhibited greater activation in the bilateral dACC/supplementary motor area, inferior parietal lobe (IPL), bilateral caudate/putamen, and visual association areas while self-evaluating on negative traits, relative to positive traits, reported higher concurrent depressive symptoms. Similarly, greater activation in the left insula during self-referential processing of negative traits, versus positive traits, was associated with higher depressive symptoms in adolescents approximately six months later. Support for the proposed neurodevelopmental model was also found, such that greater neural activation during negative self-referential processing (i.e., in the dMPFC), relative to positive self-referential processing, is related to higher concurrent depressive symptoms in early-adolescent girls, through more negative self-perception ratings during the fMRI task. Greater neural activation in the visual association area during positive self-referential processing, relative to negative self-processing, was also related to lower levels of concurrent depressive symptoms, through more positive self-perception ratings during the task. Additionally, although contrary to hypothesized associations, adolescents with greater activation during self-processing of negative traits, relative to positive, in the posterior cingulate (PCC)/precuneus, superior temporal gyrus/temporoparietal junction (STG/TPJ), and IPL reported higher social self-competence.

Preliminary results of the study indicated that, regardless of their self-perception biases or levels of depressive symptomology, early adolescent girls respond during self-referential processing of negative traits with greater activation in frontal brain regions, including the left dMPFC, VLPFC, and dMPFC/SMA, relative to positive self-referential trait processing, suggesting that, in general, early-adolescent girls recruit more self and affective neural resources when reflecting on and making negative self-evaluations, compared to positive self-judgements. The dMPFC was a hypothesized region to be important to self-referential processing. It is part of the MPFC which is believed to help regulate self-representations, as well as direct and guide attention to either internal ongoing thought or external stimuli (Davey et al., 2016; Whitfield-Gabrieli & Ford, 2012). While the VLPFC was not a hypothesized region in the current study, it is part of an emotion processing network associated with regulation of negative emotion (Casey, Jones, & Hare, 2008; Phillips, Drevets, Rauch, & Lane, 2003). In fact, the VLPFC has been associated with the regulation of negative self-beliefs using reappraisal, particularly among healthy adults, compared to socially anxious adults (Goldin, Manber-Ball, Werner, Heimberg, & Gross, 2009). Accordingly, it may be that negative self-relevant attributes may be more affectively charged and more emotionally salient, activating the dMPFC in order to support more attention to such self-representations among early adolescents. However, among relatively healthy early-adolescent girls (as in the current study), the VLPFC may play an important role in helping to regulate youths' emotional distress during negative self-referential processing, and, perhaps even, aiding in active internal regulatory responses during negative self-appraisal. Therefore, the pattern of increased recruitment seen among these youth in the dMPFC and VLPFC regions may be indicative of both greater salience of negative self-referential stimuli and a potential mechanism through which self-directed negative affect may be regulated. Adolescents also exhibited greater activation in the left and right visual association areas to both negative and positive self-relevant traits, respectively. Given the visual nature of the task, it is reasonable to deduce that both self-referential processing conditions were associated with neural activation in the visual association area, as this region is involved in orienting visual attention towards stimuli (Roelfsema, Lamme, & Spekreijse, 1998; Vorobyev et al., 2004).

In accordance with study hypotheses, adolescents' neural activation was directly associated with reports of concurrent depressive symptoms. Specifically, higher activation during adolescents' self-processing of negative traits, relative to positive traits, in the bilateral dACC/supplementary motor area, somatosensory cortex/inferior parietal lobe (IPL), bilateral caudate/putamen, and visual association areas were associated with elevated concurrent depressive symptoms. Several of these significant clusters were within or bordering the hypothesized self-referential network. Specifically, the portion of the S1/IPL cluster is within the parietal region hypothesized to be involved in integrating self and social-cognitive information into one's sense of self (Davey et al., 2016) and has been associated with self-appraisal processing and depression in adolescents and adults (Davey et al., 2017; Pfeifer et al., 2009; Silk et al., 2017). The dACC/SMA cluster also spanned into regions involved in affective salience detection (Eisenberger & Lieberman, 2004) and has been found to be activated during self-referential processing of social feedback (Olino et al., 2015; Silk et al., 2017; Silk et al., 2014), rumination regarding negative events (Burkhouse et al., 2017), and self-appraisals (Debbané et al., 2017; Pfeifer, Kahn, et al., 2013). Although not an initially hypothesized region, in this study youth with higher depressive symptoms also exhibited more activation in the caudate/putamen during negative self-referential processing. This region, along with the dACC, is involved in salience detection (Eisenberger & Lieberman, 2004; Menon, 2011), affective memory bias (Hamilton & Gotlib, 2008), and has been related to depression (Forbes & Dahl, 2012). However, greater recruitment of the caudate/putamen region has also been associated with adolescents' self-processing, relative to other person-processing (Jankowski et al., 2014; Pfeifer, Kahn, et al., 2013).

Therefore, in the context of negative self-referential processing, caudate/putamen and dACC activity may be particularly important in detecting and driving the salience of negatively charged information, while parallel activation of the PPC region may be supporting the integration of this information into adolescents' sense of self in ways that facilitate the experience of depressive symptoms. Additionally, given its involvement in affective memory bias (Hamilton & Gotlib, 2008), greater recruitment of the caudate/putamen during negative self-referential processing, compared to positive self-processing, may suggest that cognitions of negative aspects or memories related to the self are more chronically accessible (i.e., primed) in adolescents with higher depressive symptoms. Overall, these findings are consistent with previous research showing that greater activation in similar regions, particularly the ACC, caudate, and PPC during negative self-referential processing, relative to positive or a control condition, is associated with depression (Burkhouse et al., 2017; Quevedo, Ng, Scott, Smyda, et al., 2016; Silk et al., 2014). Overall, the current results indicate that negative self-relevant information may be more salient to adolescents with more symptoms of depression. The current study adds to this previous literature by explicitly investigating the relation between self-referential neural processing and depression in adolescents using a task directly designed to elicit self-referential processing, where the majority of the other studies utilized social-evaluative or affective tasks. This distinction is important as it enables more specific conclusions regarding the neural mechanisms underlying self-judgement and depressive symptomatology.

Similar to the findings with concurrent levels of depressive symptoms, findings also showed that higher activation during negative self-processing in the left insula predicted elevated symptoms in adolescents six-months later. This was not an originally hypothesized region, with respect to self-referential processing; however, the insula is a region in the affective salience network with an abundance of connections to prefrontal and parietal cortices that are related to self-referential processes (Menon, 2011; Uddin, Nomi, Hébert-Seropian, Ghaziri, & Boucher, 2017). The insula is involved in a variety of sensory, emotional, and cognitive processes, particularly with respect to the experience of negative affective states (Singer, Critchley, & Preuschoff, 2009), and is posited to modulate the function of self-referential and social cognition across the default-mode network (Frewen et al., 2020; Uddin et al., 2017). Hyperactivation of the insula in response to negative stimuli, such as social rejection/exclusion, has been associated with social distress and depression in adolescents (Masten et al., 2009; Silk et al., 2014). Therefore, youth with greater activation in the insula during negative self-referential processing may experience a higher degree of distress or pain when thinking of negative self-attributes, culminating in a vulnerability for higher depressive symptoms. These results suggest that neural functioning subserving negative self-related biases may predispose youth to an increase in depressive symptoms over time.

Findings of this study also provide evidence for the model hypothesizing that the neural underpinnings involved in processing information related to the self is indirectly related to depressive symptoms through adolescents' subjective reports of self-perceptions. Findings showed that this model was partially supported, such that adolescents' neural function in two regions, including the hypothesized dMPFC region and a visual association area, indirectly predicted concurrent depressive symptoms, but not later depressive symptoms, through adolescents' self-perception ratings during the fMRI task. Results were not found with global self-worth or social self-competence. As hypothesized, greater dMPFC activation during the negative self-referential processing, relative to positive self-referential processing, was related to higher depressive symptoms, through less positive self-perception ratings. The MPFC is posited to be one of the most important structures underlying self-referential processing, as it is found to play a key role in differentiating self and other person processing (Araujo et al., 2013; Pfeifer & Peake, 2012). Furthermore, altered activation in this region has been related to depression in adolescents and adults (Davey et al., 2017; Lemogne et al., 2010; Quevedo, Ng, Scott, Smyda, et al., 2016; Silk et al., 2017; Yoshimura et al., 2010). As mentioned earlier, the MPFC plays a role in directing and guiding attention to either internal thoughts or external stimuli and regulating sensory and semantic self-representations (Davey et al., 2016; Whitfield-Gabrieli & Ford, 2012). Therefore, it may be that greater activation in the dMPFC signals a greater shift of adolescents' attention inwards, possibly fostering the development of self-representations, during self-related processing. Accordingly, the dMPFC has been speculated to be significantly important to explicit self-focus (Frewen et al., 2020). If these functional implications are the case, youth who exhibit excessive activation in the dMPFC while self-evaluating from a *negative* perspective, more so than from a positive perspective, may have a cognitive bias or hyper-vigilance towards negative attributes of the self which are known to play a role in depressive states (Kovacs & Beck, 1978). This excessive negative self-focus may underly a greater propensity for adolescents to endorse more negative traits during self-evaluation, which in turn directly relates to higher levels of depressive symptoms at that point of time.

Additionally, greater neural activation in the visual association area during positive self-referential processing, relative to negative self-processing, was associated with lower levels of depressive symptoms, through more positive self-perception ratings during the task. Although not a hypothesized region of interest, this finding is in the hypothesized direction. As described earlier, the visual association area is important to guiding individuals' initial focus or attention to cues. Therefore, this result may indicate that the youth who have a greater initial attention bias toward positive trait words in a self-evaluation context, compared to a negative self-evaluation context, are feeling more positive about themselves in that moment, which is predictive of lower concurrent depressive symptoms. It is important to note that the indirect effects of both indirect models fell out of significance when covariates, including age, puberty, and SES, were accounted for. In these models, SES was significantly associated with the mediator (i.e., behaviorally reported self-perceptions). This resulted in reduced effects between neural activation and the mediator and outcome measure, as well as in reductions in already relatively small indirect effects. However, none of the covariates had a significant effect on the outcome measure—depressive symptoms. In contrast to hypotheses, although depressive symptoms did significantly increase from Time 1 to Time 2, indirect effects models did not predict depressive symptoms in adolescents 6-months later, maybe due to limited change in depressive symptoms across this short period.

Additionally, indirect models were not supported when using adolescents' reports of global self-worth or social self-competence as mediators. These measures of competence, although well established, assess adolescents' perceptions within these domains using very broadly worded items. For example, the Harter scale of social self-competence mainly measures adolescents' perceptions of their own popularity and ability to make friends, whereas during the fMRI self-referential task, adolescents are able to make self-evaluations on more nuanced aspects of the self that would impact how they view themselves within the context of their social relationships. Therefore, the results of these indirect models may highlight the importance of assessing self-perceptions using dynamic approaches that capture an adolescent's complex sense of self, in order to directly relate it to depressive symptoms or other behavioral outcomes.

As in previous studies (Bradley et al., 2016; Debbané et al., 2017), when assessing across the whole-brain, the current study found that adolescents' neural function during self-referential processing directly relates to their subjective reports of self-concept. These findings were specific to adolescents' in-vivo self-evaluations during the self-referential fMRI task and reports of social self-competence, but not related to global feelings of self-worth. Similar to Bradley et al. (2016), a significant association between neural function and adolescents' in-vivo ratings was found in the current study. Although in an unexpected brain region, the results were in the expected direction, showing that adolescents who exhibited greater activation in the right visual association area while evaluating themselves on *positive* traits, relative to negative traits, reported more positive ratings during the fMRI task. Given this region's involvement in initial visual attention, this may suggest that positive trait words are more salient and attention-grabbing for adolescents who are feeling more positive about themselves in the moment.

Results of the current study also revealed important associations between adolescents' neural functioning and feelings of social self-competence. However, the results were in the opposite direction of hypotheses. Findings showed that adolescents who exhibited higher activation during self-evaluation on negative traits, relative to positive traits, in the posterior cingulate (PCC)/precuneus, superior temporal/temporoparietal junction (STG/TPJ), and inferior parietal lobe (IPL) were more likely to report *higher* levels of social self-competence. Given that the fMRI task required adolescents to self-reflect on personality characteristics, findings in the resulting regions are consistent with previous research positing the important role of the PCC/precuneus to individuals' states of reflection on psychological aspects of the self (Molnar-Szakacs & Uddin, 2013) and the role of the IPL in retrieving and integrating complex semantic information into ones' sense of self (Carter & Huettel, 2013). The TPJ has been implicated in social-cognitive processes and in the integration of attention, memory, language, and perception to construct social context to guide decision making and behavior (Carter & Huettel, 2013). Additionally, results of a previous study found that the less intuitive self-appraisals are to adolescents, the more TPJ activation they recruit during self-appraisal (Pfeifer et al., 2009). Based on these functional roles, results of the current study may indicate that adolescents who generally have a positive sense of social self-competence may not be accustomed to automatically thinking of themselves from a negative perspective. Therefore, for these adolescents, more recruitment of brain activation during self-referential processing of negative traits, particularly in the PCC/precuneus and IPL clusters, may reflect a greater need for cognitive resources in order to: 1) attend to negative aspects of themselves; and 2) reference memories and self-knowledge of their behavior in social contexts to make potentially negative self-judgement ratings. It also may be that positive self-appraisals may be less demanding of neural resources in youth with higher levels of social self-competence, as they may not need to recruit these regions to reference and integrate social memories and context to make positive self-judgments. Interestingly, this possible explanation fits well with the study by Bradley and colleagues (2016) showing that, compared to healthy adolescents, depressed adolescents (who reported lower self-perception ratings than healthy adolescents) showed greater PCC/precuneus activation during self-referential processing of *positive* trait words, suggesting that greater recruitment of this region is necessary for depressed adolescents' to evaluate themselves from a *positive* perspective.

In contrast to previous work by Quevedo, Ng, Scott, Smyda, et al. (2016), no significant associations were found between adolescent neural function and subjective reports of global self-worth. Quevedo and colleagues had found that less activation in the dACC during positive trait processing, compared to negative trait processing, was associated with lower reports of self-esteem. However, the current study was conducted in a sample of early-adolescent youth with an average age of approximately 12 years, while the study by Quevedo and colleagues included girls nearly 15 years old (on average). Youth's sense of self-concept varies considerably during the highly transitional early-adolescent years (Cole et al., 2001; Wigfield et al., 1991) and overall feelings of self-concept or worth are posited to become most stable around 15 to16 years of age (Cole et al., 2001; Harter, 1999). Therefore, the lack of results in the current study with global self-worth may indicate that global self-worth has not yet stabilized enough to be directly mapped on to patterns of brain activation. Instead, it may be that, for early-adolescents, neural activation is directly related to feelings of self-competence within specific "lower-order" domains, such as the social domain as in this study, which eventually would contribute to the "higher-order" domain of global self-worth as it becomes more instantiated later in adolescence (Marsh & Shavelson, 1985).

The current study also revealed interesting effects of perceived socioeconomic status (SES). In addition to the effects of brain activation, adolescents' perceived SES was significantly related to their reports of self-perceptions during the fMRI task, social self-competence, and T1 depressive symptoms. Consistent with previous studies, including a meta-analysis (Chen & Paterson, 2006; Twenge & Campbell, 2002), adolescents who perceived their family as being higher in SES were more likely to report having more positive feelings of self-concept. Further, it was shown that youth reporting higher SES were more likely to report lower levels of depressive symptoms, consistent with previous research showing that higher subjective ratings of SES are associated with lower odds of an adolescent having a mood disorder and less hopelessness in adults (McLaughlin, Costello, Leblanc, Sampson, & Kessler, 2012; Singh-Manoux, Adler, & Marmot, 2003). In the current study, SES was measured using adolescents' subjective perceptions of their family status, regarding income, schooling, and their parents' jobs, relative to the rest of American society. Adolescents' perceptions of their family's SES were not associated with objective measures of SES, including household income and education. Therefore, these findings could indicate either that youth who perceive their family's status as higher have more positive self-perceptions and have less depressed affect, or that those who see themselves in a more positive light also tend to view their families from a more favorable perspective. Either way, overall, the results suggest that having perceptions of higher SES may be protective against lower levels of self-concept and depressive symptoms in adolescent girls.

Overall, the current study provides evidence supporting a neurodevelopmental model of self-concept and elevated depressive symptoms during the early-adolescent period. Study findings contribute to the literature by highlighting differentiated effects of negative versus positive self-referential neural processing on adolescents' subjective feeling of self-concept, particularly in the social domain. Furthermore, this is the first study to establish an indirect relationship between valenced self-referential neural processing and adolescents' depressive symptoms, through behavioral reports of adolescent self-perceptions, providing more insight into how brain-behavior connections may play a role in depressogenic affect. Despite these exciting findings, the study had several limitations. First, the sample was limited to girls. Although girls are at highest risk for depression during adolescence (Costello et al., 2003), findings may not generalize to boys as there may be differences between boys and girls in which domains of self-concept are most important to sense of self, and, in turn, possibly more important to risk for depression. For example, early adolescent boys tend to positively regard themselves in the athletic and physical appearance domains (Cole et al., 2001), therefore, feelings of competence within these areas may be more appropriate than to social self-competence to test as mediators in the proposed model for boys.

In addition, the sample of girls included in the study reported relatively low levels of depressive symptoms at both time points. Although depressive symptoms significantly increased over the six-month span between assessments, on average, girls' symptoms levels were not within the clinical range. This is not necessarily a negative of the study, as the neurodevelopmental model was intended to predict risk or vulnerability for depression. However, this may have limited the ability to predict increases in depressive symptoms longitudinally in the indirect effect models, as there may not have been large enough variability between the timepoints for some youth. Previous research has suggested that depression rates do not peak until ages 15 or 16 (Costello et al., 2003), therefore, the longitudinal models may have been more robust in detecting future risk for depression with assessments of girls' depressive symptoms a few years later. Even so, the current study did provide a first step in highlighting how adolescents' neural self-referential processing is indirectly related to concurrent depressive symptoms, through their in-the-moment self-perceptions. Unfortunately, given that the predictor and mediator were measured within several weeks of each other, and the predictor and outcome measures were measured at the same visit, causality of effects cannot be concluded. Therefore, it could be that adolescents who have more negative self-perceptions are more attentive towards their own negative attributes, which is influencing their neural processing patterns during self-evaluation. Future research should be done to replicate the current findings and assess the longitudinal models using larger samples and multiple timepoints across longer periods throughout adolescence. In addition, many tests were conducted assessing for indirect effects. However, this study aim was somewhat exploratory in nature, as it was the first to assess how brain function among several regions might influence depression through several markers of subjective self-concept during adolescence. Therefore, multiple comparison corrections were not conducted for indirect effect analyses; however, the results are limited, as there was a potential for Type 1 error.

A strength of the Self versus Change task was that it enabled the assessment of differences in adolescents' processing of negative versus positive self-referential neural processing. However, the task was programmed such that interstimulus interval periods (i.e., ISI; the time between each trait word/evaluation presentation) was quite abbreviated, and positive and negative trials were randomly distributed across the task (i.e., not presented in blocks). Therefore, this short ISI could be viewed as providing insufficient time between trials to allow for the hemodynamic response to return close enough to baseline. This would mean that BOLD response for each trait word would not be able to be adequately differentiated, muddling the ability to detect trial-type effects. This, however, could mean that the results found may be conservative estimates of true associations between differential neural response and the measures of self-concept and depression.

Finally, the current study results were conducted using a whole-brain approach, rather than the originally proposed approach of examining results only within an a priori, self-referential region mask. When using the masked approach, only one significant cluster of activation was found in the entire study, which correlated self-referential processing of negative traits in the precuneus with adolescents' social self-competence. However, upon further investigation, several clusters found using the whole-brain approach either bordered or overlapped regions within the a priori mask. For instance, the cluster in the left dMPFC that was shown to be more activated during self-negative processing, relative to positive, across the entire sample and had indirect effects on depressive symptoms through the effects of adolescents' self-perceptions was in fact overlapping with hypothesized areas in the mask. Similarly, when correlating neural activity to social self-competence, other than the precuneus region that was found to be significant using the mask, a small portion of the STG/TPJ cluster found in the whole-brain analyses also overlapped within the a priori areas defined by the self-referential mask. Finally, when associating neural activity with concurrent depressive symptoms, portions of the dACC/SMA and PPC clusters overlapped with a priori regions in the mask. Therefore, it is likely that fMRI analyses were not significant when conducted within the originally proposed self-referential processing mask because clusters of activation specifically found within the regions of the mask were not large enough to pass significance thresholds.

Given the paucity of research addressing direct associations between neural self-referential processing and adolescent-reported self-perceptions, the findings of this study make a valuable contribution to the literature about how differential neural processing of negative versus positive self-relevant information directly maps onto behavioral reports of self-concept during adolescence. Furthermore, the findings highlight a potential neurodevelopmental model in which neural patterns of self-referential processing confer risk for elevated depressive symptoms through concurrently reported self-perceptions during early adolescence. Given that early adolescence is an important developmental period in which self-concept and risk for depression begin to develop (Costello et al., 2011; Shapka & Keating, 2005), the current study presents a nuanced model that begins to elucidate potential underlying mechanisms through which adolescents' neural functioning in relation to self-reflection on negative and positive characteristics contribute to subjective feelings of self-competence/perceptions and depressive symptomatology. Very recent research has started to establish the use of neurofeedback paradigms that engage self-focused processing (i.e., happy self-face stimuli) for depressed adolescents (Quevedo et al., 2019). Therefore, research findings such as those of the current study may help to play a role in the continued development of novel neurofeedback interventions by offering insight on specific neural targets that could help in the reduction of negative self-perceptions and, in turn, depressive symptoms in adolescents.

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